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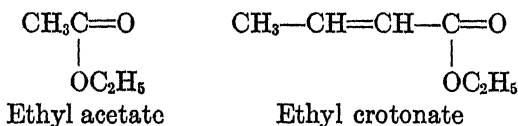
THE PRINCIPLE OF VINYLITY

REYNOLD C. FUSON

Department of Chemistry, University of Illinois, Urbana, Illinois

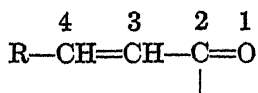
Received December 20, 1934

It has long been recognized that, in a molecule containing a system of conjugated double linkages, the influence of a functional group may sometimes be propagated along the chain and make itself apparent at a remote point in the molecule. For example, the methyl group in ethyl crotonate behaves in some respects as it does when it is attached directly to the ester group as in ethyl acetate.



Similarly, the methyl group in *p*-nitrotoluene resembles that in *o*-nitrotoluene, and both of these groups resemble the methyl group in nitromethane, which is attached directly to the nitro group. It is as though the influence of the nitro group were felt even when the methyl group is located in a distant part of the molecule.

Another characteristic property of conjugated systems is that in addition reactions the extremities of the system may be involved even though they be widely separated. The 1,4-addition of certain reagents to α, β -unsaturated ketones and esters is an example. In these cases, carbon atom 4 may be said to usurp the function of carbon atom 2:



Phenomena of the foregoing general types have been effectively correlated by many authors, notably Angeli (2, 3), Lapworth (50), Koenigs (44), Thiele (70), and Claisen (17), who have dealt with the problem primarily on an empirical basis. Others, especially in recent years, have, by reference to theoretical considerations, succeeded in greatly clarifying the problems involved.¹

¹ See, for example, Robinson: *J. Soc. Dyers Colourists Jubilee Journal*, 65 (1934).

Examples of such effects have increased rapidly in variety as well as in number, and it seemed worth while to attempt to formulate an expression which would make the significance of this wealth of material more readily apparent. The present review is presented as a contribution to this problem. An empirical principle has been worked out which is designed to embrace a wide variety of phenomena and which, at the same time, can be stated in relatively simple terms.

If E_1 and E_2 be made to represent non-metallic elements, the generalization takes the following form: *When, in a compound of the type $A-E_1=E_2$ or $A-E_1\equiv E_2$, a structural unit of the type $-(C=C)_n-$ is interposed between*

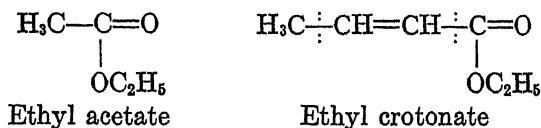
A and E_1 the function of E_2 remains qualitatively unchanged but that of E_1 may be usurped by the carbon atom attached to A. The resulting compound will have the form $A-(C=C)_n-E_1=E_2$ or $A-(C=C)_n-E_1\equiv E_2$, and in

any given series of this type the members will differ from each other by one or more vinylene residues.² It is proposed to term such a group of compounds a vinylogous series. The members of a vinylogous series will then be vinylogs of one another.³

In what follows, a number of different vinylogous series are pointed out and, in each case, illustrative reactions have been cited to show the application of the general principle under consideration. In view of the fact that each of these classes represents a broad field of study, it has not seemed desirable in any instance to attempt an exhaustive review of the literature.

ESTERS

In this series the operation of the principle of vinylogy may be illustrated by a comparison of the esters of saturated fatty acids with their vinylogs, the α , β -unsaturated esters. Ethyl acetate and ethyl crotonate may be



used as typical examples. In each case $A = \text{CH}_3$ and $E_1=E_2$ is $-\text{C}=\text{O}$.

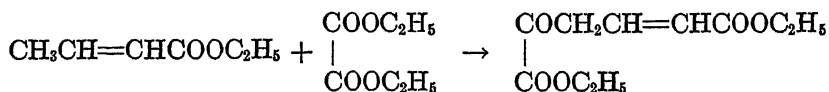


In the first $n = 0$; in the second $n = 1$. A function of the carbonyl carbon atom in ethyl acetate (acting in conjunction with the carbonyl oxygen

² It is understood, of course, that the vinylene residues will be disposed in a linear arrangement.

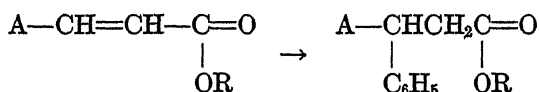
³ The term "vinylene homologs" has been used to designate the simplest type of vinylogs, namely, those differing by $-(\text{CH}=\text{CH})_n-$, i.e., one or more *unsubstituted* vinylene groups. See, for example, König: Ber. 55, 3297 (1922).

atom) is to activate the hydrogen atoms of the methyl group attached to it. In ethyl crotonate this function is usurped by the carbon attached to the methyl group (A). Thus, ethyl crotonate condenses with ethyl oxalate (50) in a manner which is analogous to the behavior of ethyl acetate under similar conditions (78):

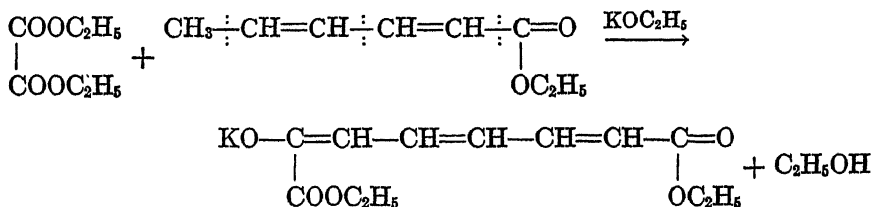


Ethyl β -ethoxycrotonate behaves similarly (81).

Again, when phenylmagnesium bromide is added to saturated esters the phenyl group becomes attached to the carbon atom of the carbonyl group; in α , β -unsaturated esters the phenyl group may attach itself instead to the carbon atom in position 4, i.e., to the carbon atom joined to A (45):

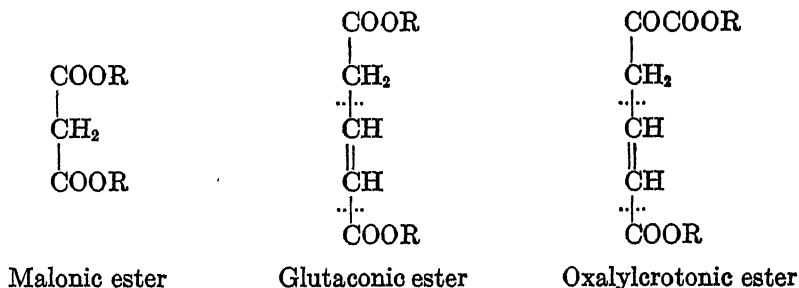


It has recently been shown that the next higher vinylog ($n = 2$), ethyl sorbate, also has an active methyl group. Like the acetic and crotonic esters, it condenses with ethyl oxalate (15):



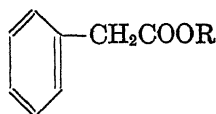
Sorbic ester also undergoes 1,6-addition (25, 12). It will be seen that in both of these types of reaction the function of the carbon atom of the carbonyl group has been usurped by that adjoining the group which corresponds to A in the general formula.

Among esters of dibasic acids, glutaconic ester and oxalylcrotonic ester are recognizable as vinylogs of malonic ester:

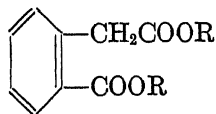


In reactions with alkylating agents (33, 11), diazo compounds (60), and other reagents the behavior of the methylene group in these esters shows a very close parallel to that of the malonic esters.

Similarly, the methylene group in the esters of homophthalic acid is known to be very much more reactive than that of the phenylacetic esters (21, 20):

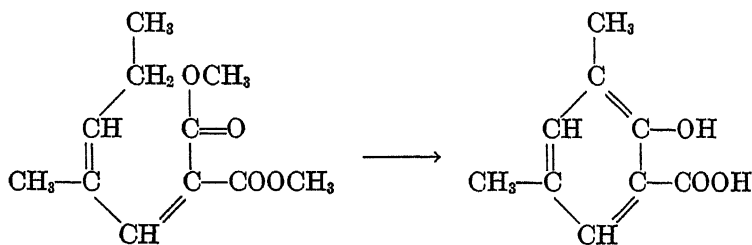


Phenylacetic ester

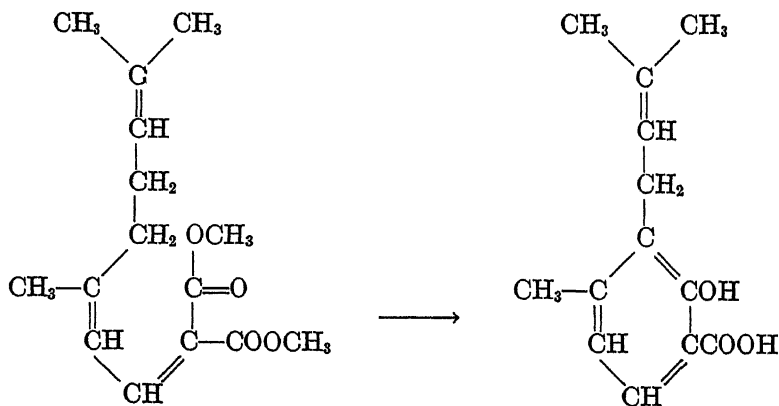


Homophthalic ester

Meerwein's conversion of dimethyl α -methyl- β -ethylacrylidene malonate and dimethyl citralidenemalonate into the corresponding derivatives of salicylic acid illustrates the behavior of the next higher vinylogs (55):



Dimethyl
 α -methyl- β -ethylacrylidene malonate

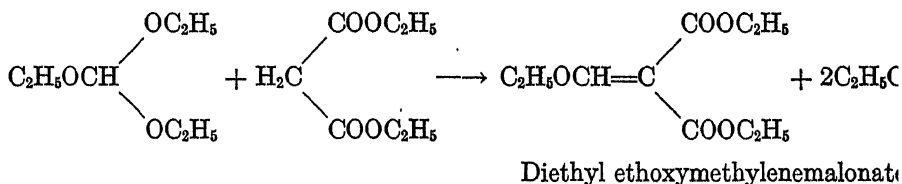


Dimethyl
citralidenemalonate

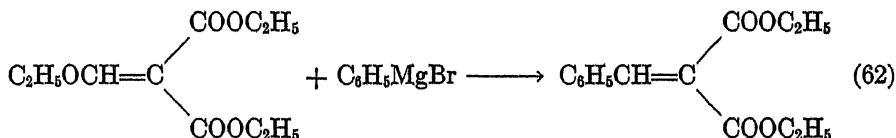
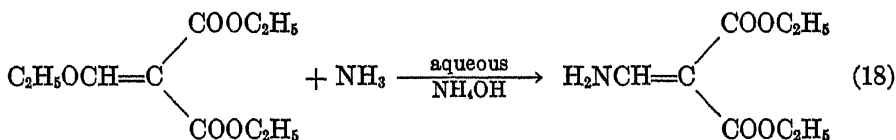
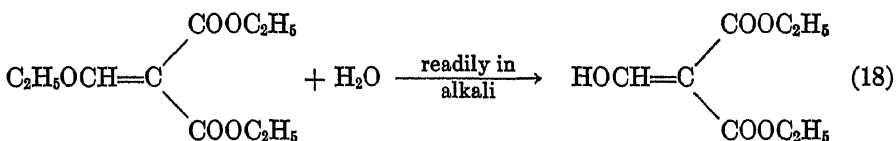
The latter case is of particular interest, inasmuch as the ester contains a methyl as well as a methylene group in position to condense with the carbomethoxyl group. It seems probable that the course of the ring-closure may depend on the configuration of the ester. Moreover, it may be that negative results in similar cases (19, 55) may be explained by assuming an unfavorable configuration.

β-Alkoxyacrylic esters

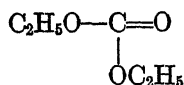
The alpha-substituted β-alkoxyacrylic esters which form when ethyl acetoacetate, ethyl cyanoacetate, and similar substances are condensed with orthoformic ester behave in a manner which has long been regarded as anomalous. As an example may be cited diethyl ethoxymethylenemalonate which is formed according to the following equation:



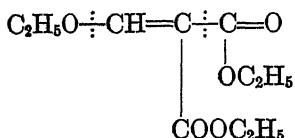
Among the peculiar reactions of this substance are the following:



The great ease with which the ethoxyl group suffers direct replacement by the hydroxyl, amino, and phenyl groups in the above reactions ceases to appear anomalous when we reflect that we are dealing with a vinylog of diethyl carbonate:

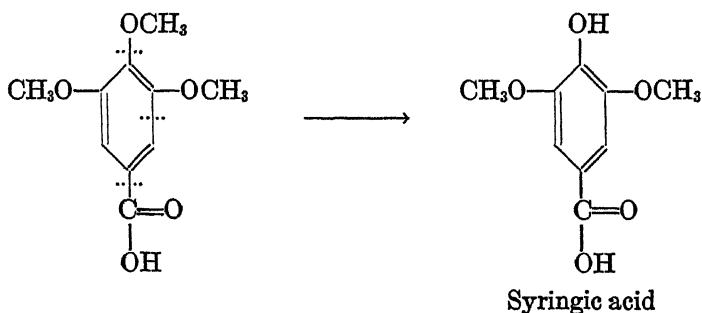


Diethyl carbonate

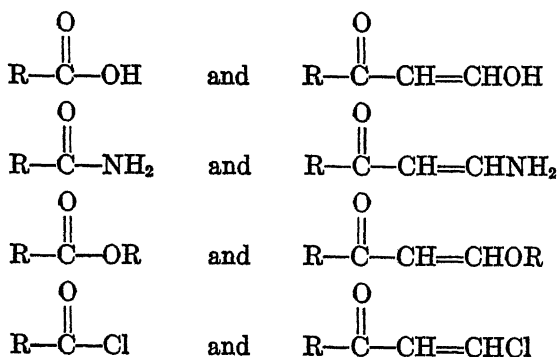


Diethyl ethoxymethylenemalonate

This principle suggests that *o*- and *p*-alkoxybenzoic acids would undergo cleavage more readily than would the corresponding meta derivatives. The conversion of 3, 4, 5-trimethoxybenzoic acid into syringic acid (31, 32) is in accord with this point of view, for the trimethoxyl compound is vinylogous with carbonic ester only with reference to the methoxyl group in position 4:



This general point of view has been elaborated by Claisen (17, 4), who pointed out certain similarities between the following pairs of structures:

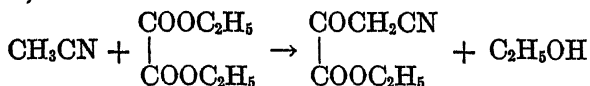


NITRILES

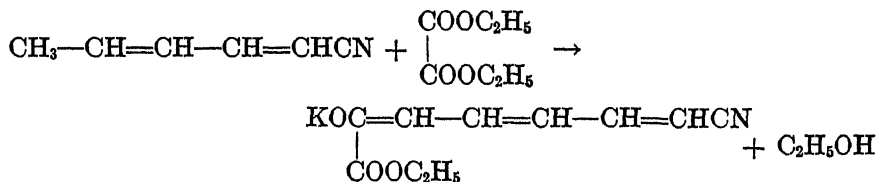
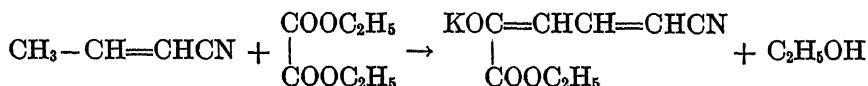
Acetonitrile, crotonitrile, and sorbic nitrile form a vinylogous series in which the activity of the hydrogen atoms of the methyl group is qualitatively independent of *n*.



In this series $A = \text{CH}_3$, $E_1 = \text{C}$, and $E_2 = \text{N}$. It has long been known that acetonitrile condenses with oxalic ester in the presence of sodium ethoxide (28):

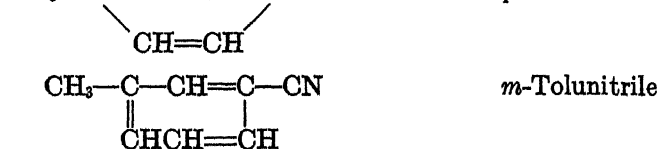


Borsche and Manteuffel (16) have recently shown that, by using potassium ethoxide, a similar result is obtained with crotonitrile and sorbic nitrile:

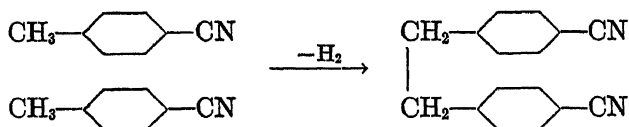


The term vinylogous series has been defined in such a manner as to include many of the correlations which have been made by Angeli, whose celebrated rule (3) states that in ortho- and para-disubstituted benzene derivatives ($A\text{—C}_6\text{H}_4\text{—B}$) the substituents (A and B) react as though the benzene ring were not present (i.e., as $A\text{—B}$). This rule was extended to include compounds of more complex types, such as $A\text{—C}_6\text{H}_4\text{—C}_6\text{H}_4\text{—B}$, $A\text{—C}_6\text{H}_4\text{CH=CHC}_6\text{H}_4\text{—B}$ and $A\text{—C}_6\text{H}_4\text{N=NC}_6\text{H}_4\text{—B}$, as well as groups separated by an unsaturated chain.

In the vinylogous series under discussion would also be included *o*- and *p*-tolunitrile, but not the meta isomer.



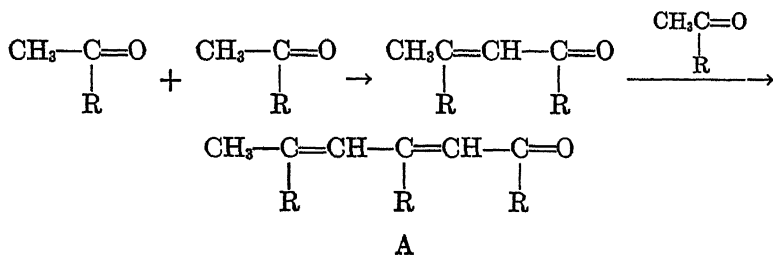
The implication of the generalization under consideration, as well as that of Angeli, is that in the *o*- and *p*-tolunitriles the activity of the hydrogen atoms of the methyl groups will be greater than that of the corresponding atoms in toluene or in *m*-tolunitrile. Some evidence is at hand in support of this. Kattwinkel and Wolfenstein (41) found that when *p*-tolunitrile is oxidized with potassium or ammonium persulfate, 4,4'-dicyanodibenzyl results:



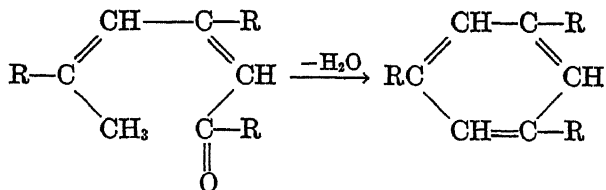
The meta isomer does not undergo this reaction.

KETONES

It seems probable that the formation of mesitylene and other 1,3,5-trialkyl- and triaryl-benzenes depends on the activation of a methyl group joined to a ketone group by a butadiene chain. By condensing together in a linear fashion three molecules of a methyl ketone we would get a vinylog (A) of the parent ketone:

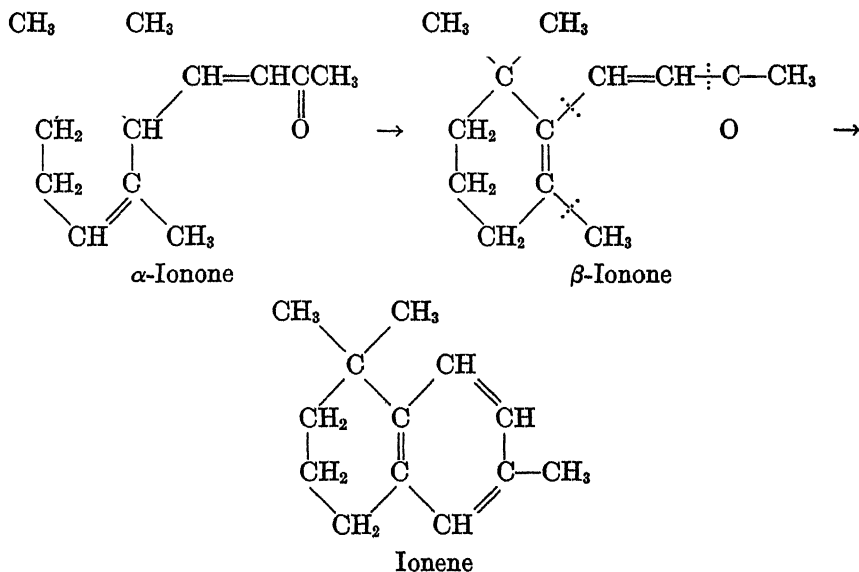


The cyclization may then be formulated as an intramolecular condensation which depends on the activity of the methyl group of this vinylog:



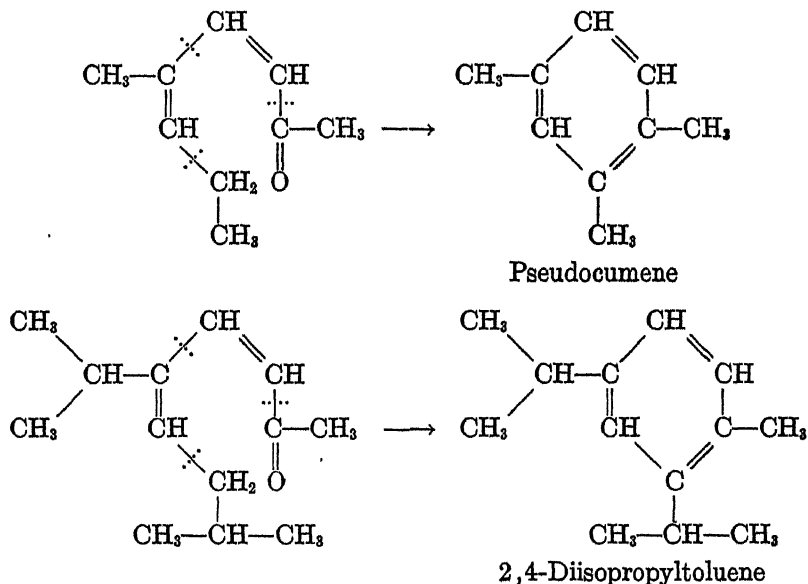
The transformation of α - and β -ionone into ionene is an example of a similar condensation. Bogert and Fourman (13) have recently shown the correctness of Barbier and Bouveault's (8) structure for ionene as opposed to the earlier structure proposed for this hydrocarbon by Tiemann and

Kruger (73, 74). The new structure permits a formulation of the condensation as that of a vinylog of acetone:



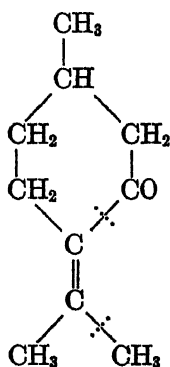
In the case of α -ionone the first step in the condensation would be the isomerization to the beta isomer.

Barbier and Bouveault's syntheses of pseudocumene and 2,4-diisopropyltoluene rest on condensations similar to that indicated for ionene (7):



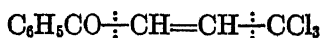
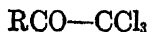
When we consider the configurational possibilities of an open chain molecule containing two ethylenic linkages, it is not surprising that ring-closures of this type frequently fail to take place. Examples are Dautwitz's failure to obtain *p*-xylene from acetone and tiglic aldehyde (19), and Kekulé's unsuccessful attempt to obtain benzene by cyclization of sorb-aldehyde (42).

Poggi's discovery that pulegone gives the iodoform test (59) is interesting in view of the fact that this ketone is vinylogous with methyl ketones.



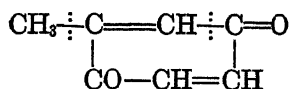
Pulegone

It is possible that a trichloromethyl derivative is formed as an intermediate. This suggests that compounds such as trichloroethylideneacetophenone (43), which are vinylogous with trichloromethyl ketones, might undergo cleavage with alkali to give chloroform:



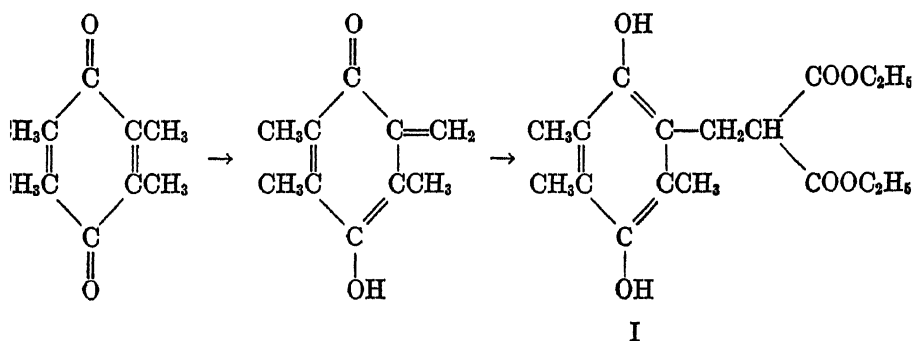
QUINONES

Methylquinones are vinylogous with methyl ketones and might, therefore, be expected to have active methyl groups:

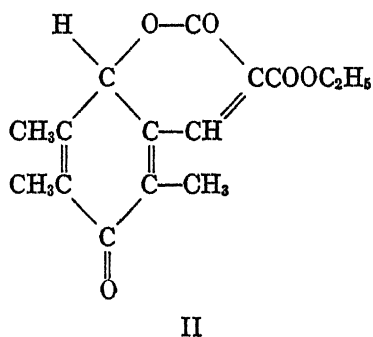


The peculiar condensation of malonic ester with duroquinone observed by Smith and Dobrovolny (69, 68) indicates that one of the methyl groups of the quinone is active. The following is a possible mechanism based

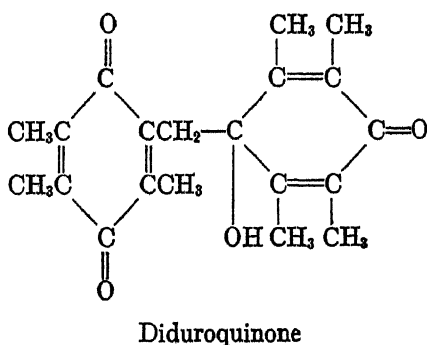
upon the assumption that the hydrogen atoms of the methyl groups are sufficiently mobile to undergo a 1,4-prototropic shift:



By a process involving oxidation, a succession of prototropic changes, and a ring-closure, the final product (II) may be produced from I.

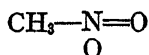


It seems likely also that a methyl group is involved in the dimerization of certain methylquinones. Thus Rügheimer and Hankel (63) write diduroquinone as follows:

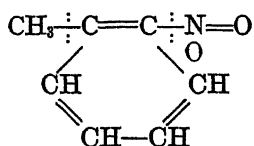
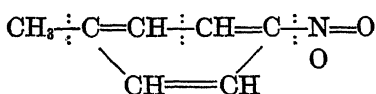
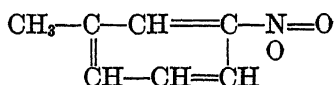


NITRO COMPOUNDS

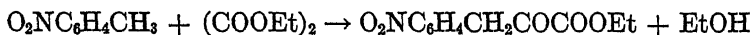
Among nitro compounds may be cited nitromethane, *o*-nitrotoluene, and *p*-nitrotoluene (but not *m*-nitrotoluene), which form a vinylogous series in which A = CH₃, E₁ = N, and E₂ = O.



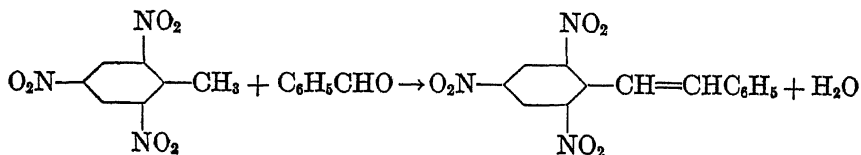
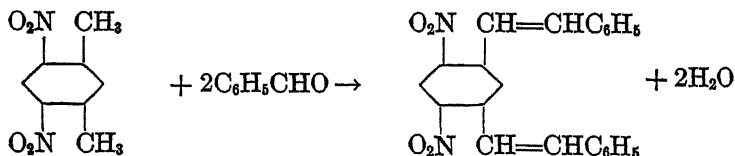
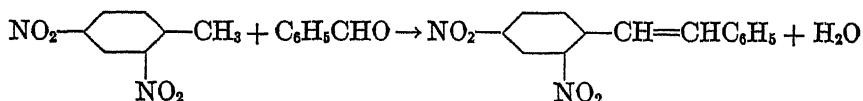
Nitromethane (n = 0)

*o*-Nitrotoluene (n = 1)*p*-Nitrotoluene (n = 2)*m*-Nitrotoluene

As is well known, the methyl group in nitromethane enters into a wide variety of reactions involving the removal of one or more of its hydrogen atoms (34, 71). As has been repeatedly pointed out by Angeli and others, the *o*- and *p*-nitrotoluenes, in contrast to the meta isomer, undergo similar reactions. With diethyl oxalate, for example, they yield keto esters (61):

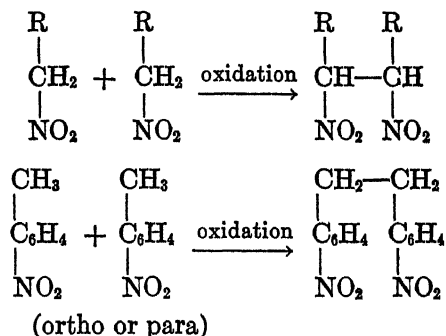


2,4-Dinitrotoluene (72), 4,6-dinitro-*m*-xylene (14), trinitrotoluene (58), and other similarly constituted compounds behave analogously when treated with benzaldehyde:

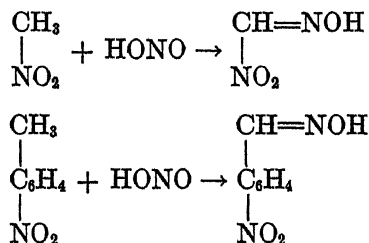


Similar results are obtained by the use of nitroso compounds in place of benzaldehyde (65).

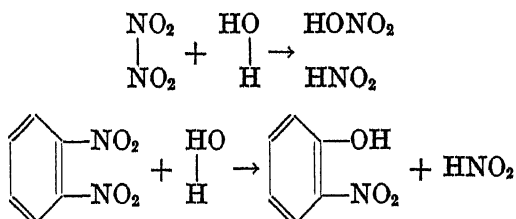
An extremely interesting comparison of these vinylogs was made by Angeli (5), who pointed out that in each case it was possible to effect coupling by oxidation:



Angeli (1) showed also that *p*-nitrotoluene was converted by the action of nitrous acid to the oxime analogous to the nitrolic acid derived from nitromethane in the same manner:

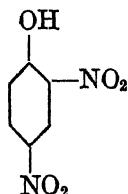


Angeli has also noted the interesting parallel between nitrogen peroxide and its vinylogs. The hydrolysis of nitrogen peroxide shows a formal similarity to that of *o*- and *p*-dinitrobenzene:



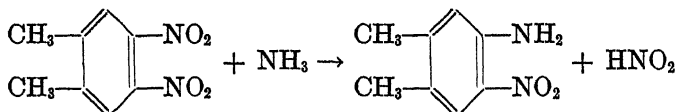
The replacement of a nitro group in *o*-dinitrobenzene by a hydroxyl group (51), an amino group (52), or a methoxyl group (54) takes place when the dinitro compound is treated, respectively, with aqueous alkali, ammonia, or sodium methoxide. Similar reactions take place with *p*-dinitrobenzene (54). *m*-Dinitrobenzene, on the other hand, resists the action of such

reagents; heating with solid potassium hydroxide fails to displace the nitro groups. Wohl (82) showed that in this case the product was 2,4-dinitrophenol:



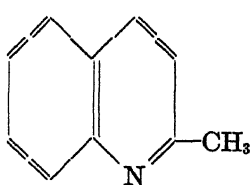
2,4-Dinitrophenol

This behavior of *o*- and *p*-dinitrobenzene is general (53). Thus Kuhn, Reinmund, and Weygand (47) carried out the following replacement:

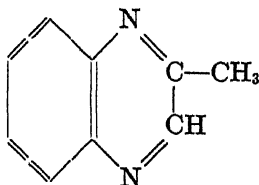


SIDE-CHAIN ACTIVATION IN THE PYRIDINE SERIES AND IN RELATED COMPOUNDS

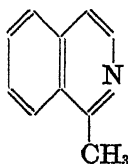
The imino group ($-\text{C}=\text{N}-$), which forms a part of many heterobenzenoid rings, may fulfill the function of $\text{E}_1 = \text{E}_2$. This is demonstrated by the fact that the methyl groups in quinaldine (77, 39), 2-methylquinoxaline (10), 1-methylisoquinoline (57), 2-methyl-4-phenylthiazole (57), and similar substances containing the structural unit $\text{CH}_3-\text{C}=\text{N}-$, are much more reactive than in such compounds as 3-methylquinoline and 2-phenyl-4-methylthiazole in which this structural unit is not present:



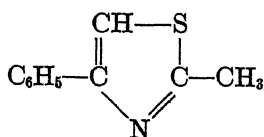
Quinaldine



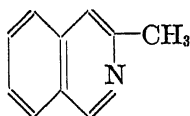
2-Methylquinoxaline



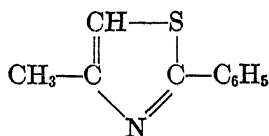
1-Methylisoquinoline



2-Methyl-4-phenylthiazole

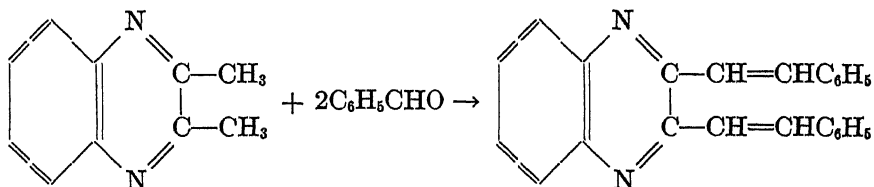


3-Methylisoquinoline



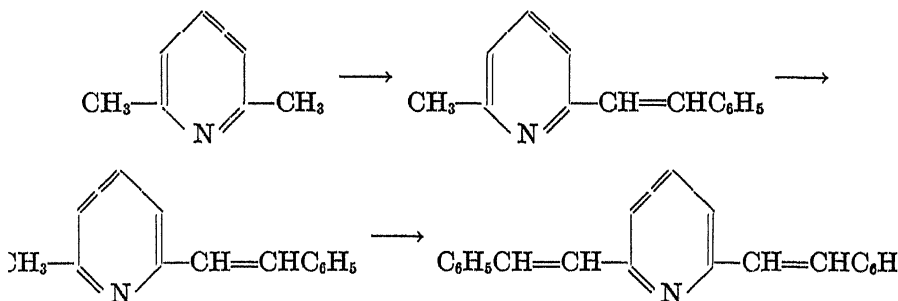
2-Phenyl-4-methylthiazole

Perhaps the most characteristic reaction of active methyl groups in such compounds is the formation of benzal derivatives by interaction with aromatic aldehydes in the presence of a suitable catalyst such as zinc chloride. It has been found that in 2,3-dimethylquinoxaline (10) and α, α' -dimethylpyridine (67) both methyl groups are active; in each case a dibenzal derivative may be prepared:



2,3-Dimethylquinoxaline

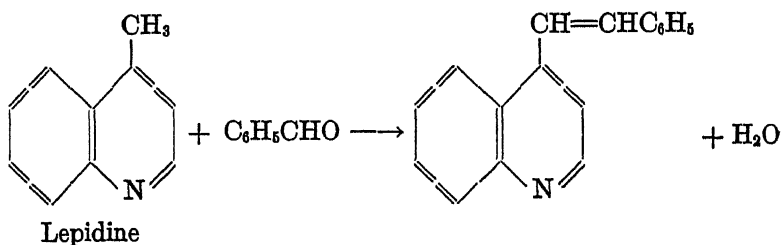
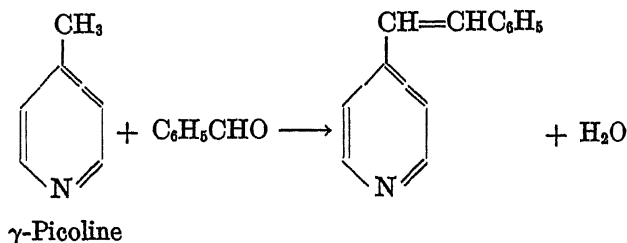
In the case of α, α' -dimethylpyridine the condensation may be assumed to proceed in two steps and to involve a shift of the double bonds in the benzenoid nucleus:



It is interesting to note, however, that according to the principle of vinyl-ogy both methyl groups may be active without any shift of double bonds.

In all of these compounds $A = \text{CH}_3$, $E_1 = \text{C}$, $E_2 = \text{N}$, and $n = 0$. Examples of the next higher vinylog ($n = 1$) are γ -picoline and lepidine. In accordance with the implications of the fact that these compounds are vinylogous with α -picoline and quinaldine, the methyl groups are found to

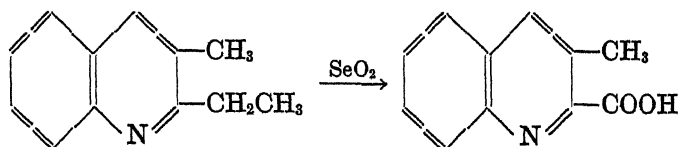
show the same type of reactivity. γ -Picoline (29) yields a benzal derivative when treated with benzaldehyde. Lepidine behaves similarly (23).



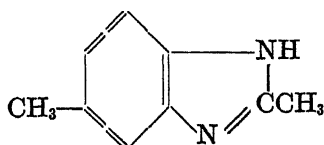
With *p*-chlorobenzaldehyde lepidine gives a 70 per cent yield of *p*-chlorobenzallepidine (30). When treated with benzaldehyde 2-phenyllepidine gives a 54 per cent yield of the corresponding benzal derivative (40).

The fact that a methyl group will be reactive if located in the α - or γ -positions of the pyridine ring and inactive if situated in the corresponding β -position was early recognized by Koenigs (44) and is frequently spoken of as Koenigs rule. It is evident that, so far as concerns compounds of this type, this rule is equivalent to the principle under discussion.

An interesting observation, which illustrates this rule, has recently been made by Henze (35). Henze found that in the oxidation of 2-ethyl-3-methylquinoline with selenium dioxide the ethyl group is attacked preferentially:

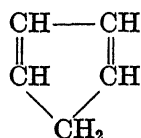


Similarly, it was found by Wislicenus and Kleisinger (80) that quinaldine and lepidine react with oxalic ester to give the corresponding α -keto esters. β -Methylquinoline, on the other hand, is unreactive toward oxalic ester (79). Another example is furnished by α , *m*-dimethylbenzimidazole in which only the α -methyl group condenses with benzaldehyde (6):

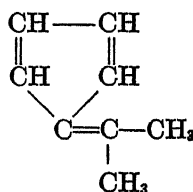
*α, m*-Dimethylbenzimidazole

CYCLOPENTADIENES

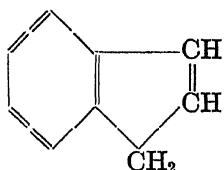
Cyclopentadiene, indene, and fluorene may be regarded as the initial ($n = 0$) members of a vinylogous series in which the corresponding dimethylfulvenes exemplify the next higher member ($n = 1$):



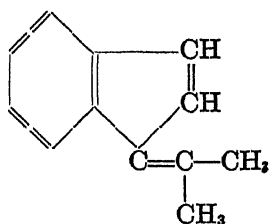
Cyclopentadiene



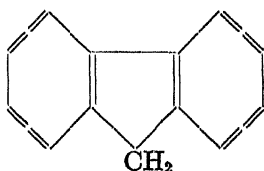
Dimethylfulvene



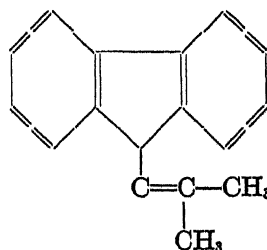
Indene



Dimethylbenzofulvene



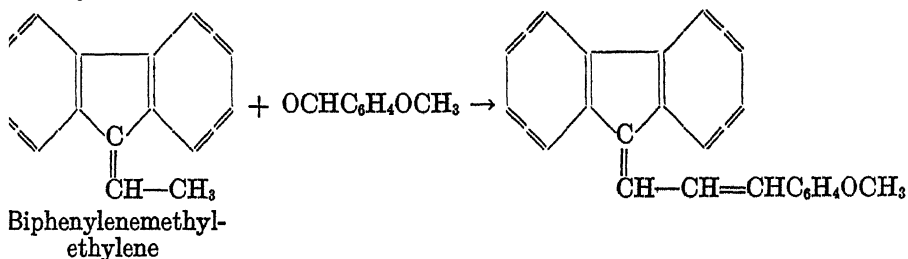
Fluorene



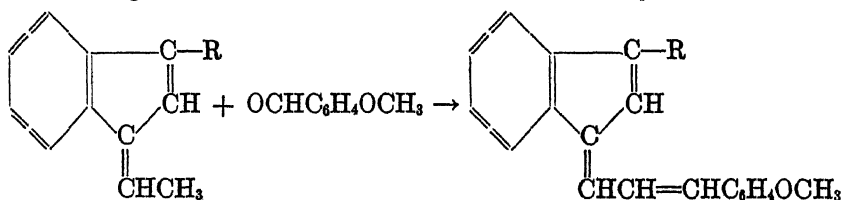
Biphenylenedimethylethylene

Schlenk and Bergmann (66) have shown that the peculiar activity of the hydrogen atoms of the methylene group characteristic of the first members of this series is present also in the higher vinylogs. These act upon sodium triphenylmethyl to convert it to triphenylmethane, thus behaving as compounds possessing active hydrogen atoms.

More recently Ziegler and Crössmann (83) have been able to confirm this viewpoint by effecting a condensation between biphenylenemethylethylene and anisaldehyde:

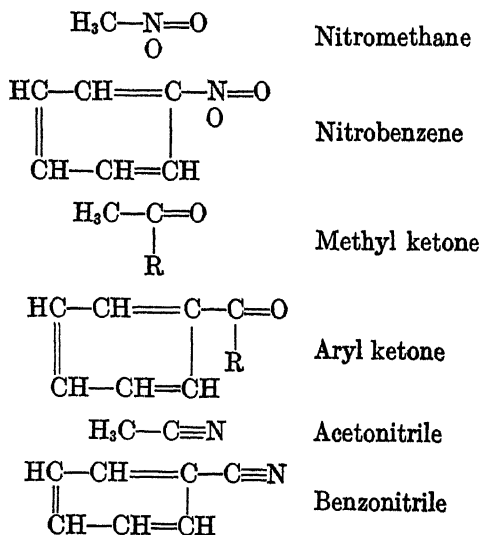


The analogous reaction was also effected in the indene system:



THE INTRODUCTION OF GROUPS INTO THE META POSITION IN MONOSUBSTITUTED BENZENE DERIVATIVES

In view of the fact that such groups as $-\text{NO}_2$, $-\text{COR}$, and $-\text{C}\equiv\text{N}$ when present as substituents on a benzene ring direct entering substituents preferentially to the meta position, it is interesting to note that such benzene derivatives may be regarded as vinylogs, respectively, of nitromethane, methyl ketones, and acetonitrile:



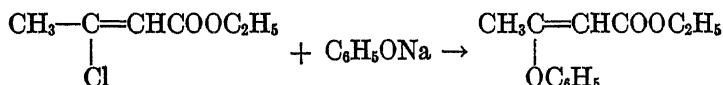
From this point of view one might expect the hydrogen atoms in the meta positions to be more active than those in ortho and para positions. In fact, Lapworth was led to his discovery of the activity of the gamma hydrogen atoms of crotonic ester through a consideration of the structural similarity of this ester to benzoic ester (50).

ACTIVATION OF HALOGENS IN VINYLOGOUS SYSTEMS

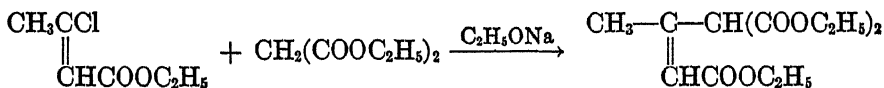
In vinyl halogen compounds such as chlorobenzene and chloroethylene the halogen atom is relatively unreactive, and this sluggishness in entering into reaction has come to be regarded as normal for compounds having the

structural unit $\begin{array}{c} \text{C}=\text{C}-\text{X} \\ | \\ \text{R} \end{array}$. However, there are notable exceptions and

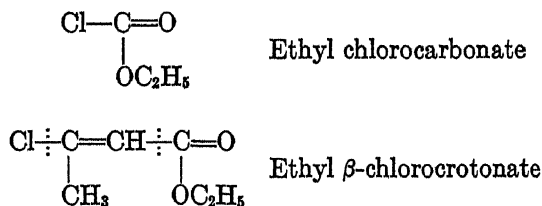
these have, of course, been looked upon as anomalous. Perhaps the simplest example is ethyl β -chlorocrotonate. Ruhemann and Wragg have shown that with sodium phenoxide this ester suffers replacement of its halogen atom by the phenoxy group (64):



Similarly, Fichter and Schwab (27) were able to condense the chloroester with malonic ester:

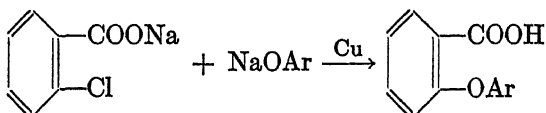


The unexpected reactivity of the chlorine atom is, however, readily explained on the basis of the vinylogous relationship between ethyl β -chlorocrotonate and ethyl chlorocarbonate:

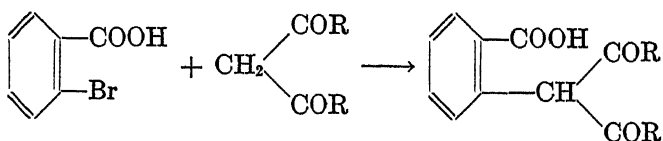


The foregoing example is only one of a wide variety of halogen derivatives in which an active halogen atom is attached to the vinyl grouping. This group of substances can be conveniently related to the numerous active methyl derivatives already considered by reference to the rule that when an active methyl group is replaced by a halogen atom the halogen atom will be active.

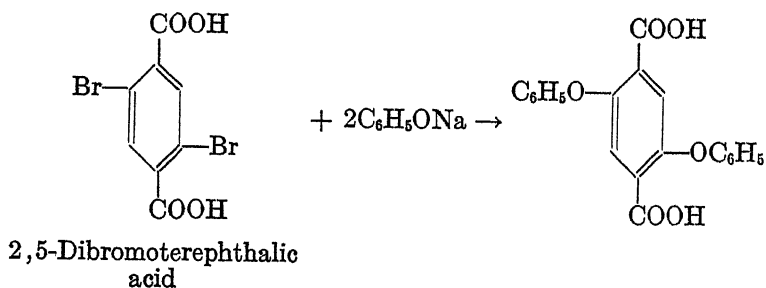
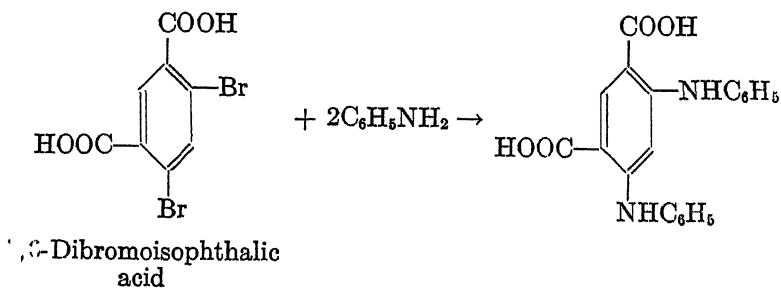
Another example of the same sort is the replacement of the halogen atom in *o*-bromo- and *o*-chloro-benzoic acids. Thus Ullmann and Zlokasoff showed that when sodium *o*-chlorobenzoate is treated with sodium phenoxides in the presence of copper it gives the corresponding aryl ethers of salicylic acid (76):



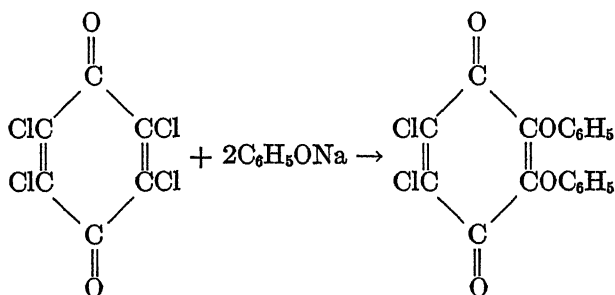
Similarly, *o*-bromobenzoic acid reacts with active methylene compounds in the following fashion (36):



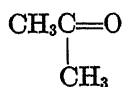
Eckert and Seidel (24) studied the replaceability of the bromine atoms in 4,6-dibromoisophthalic acid and 2,5-dibromoterephthalic acid. In both instances the halogen atoms are readily replaceable by anilino and phenoxy residues:



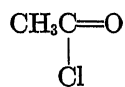
The replacement of the halogen atoms in the anils is a similar reaction (38):



The following list of pairs will make clear the application of the rule:



Acetone



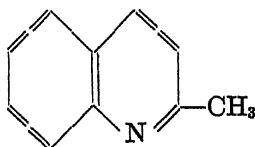
Acetyl chloride



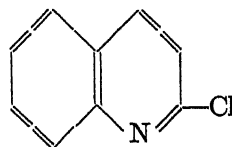
Acetonitrile



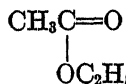
Cyanogen bromide



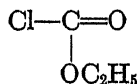
Quinaldine



2-Chloroquinoline

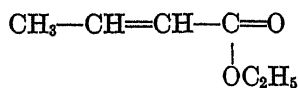


Ethyl acetate

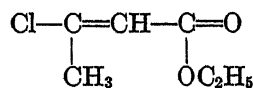


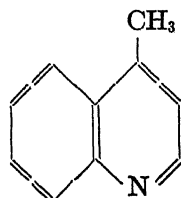
Ethyl chlorocarbonate

The rule holds equally well for compounds vinylogous with the above types.

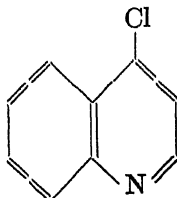
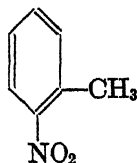
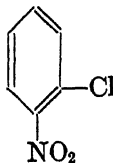


Ethyl crotonate

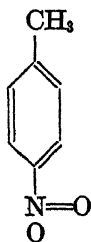
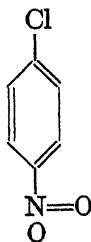
Ethyl β -chlorocrotonate



Lepidine

 γ -Chloroquinoline*o*-Nitrotoluene*o*-Chloronitrobenzene

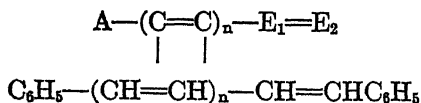
An example of the next higher vinylog is *p*-nitrotoluene; in accordance with prediction, the chlorine atom in *p*-chloronitrobenzene is active.

*p*-Nitrotoluene*p*-Chloronitrobenzene

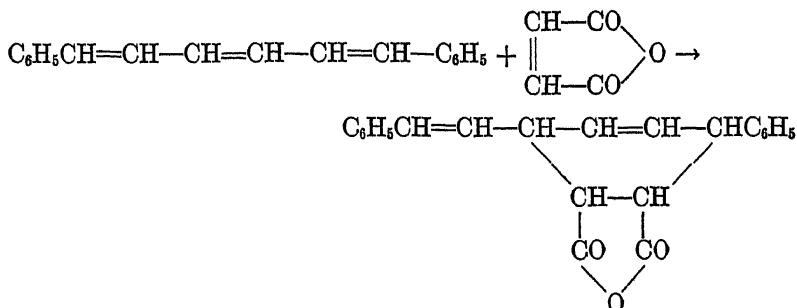
ADDITION REACTIONS OF VINYLOGOUS COMPOUNDS

That the 1,2-addition which is characteristic of compounds of the type $A-E_1=E_2$ is frequently supplanted by 1,4-addition in the next higher vinylog, $A-C=C-E_1=E_2$, is another example of a way in which the carbon atom joined to A may usurp the function of E_1 . Examples of 1,6, 1,8, 1,10 and similar types of addition reactions illustrate the behavior of the higher vinylogs.

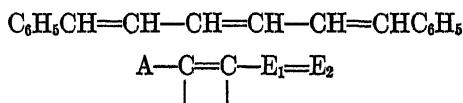
The diphenylpolyenes prepared by Kuhn and Winterstein (49) are of especial interest. They constitute a vinylogous series in which $A = C_6H_5$, $E_1 = C$, and $E_2 = C$:



It is to be noted that when the vinylogs in which n is greater than 1 are condensed with maleic anhydride the reaction is always of the 1,4 type, even when the formation of a larger ring is possible (26, 22, 48):

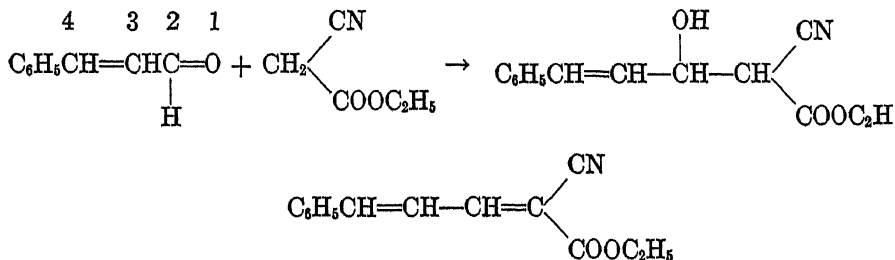


In order to interpret this result according to the principle of vinylogy we must set A equal to $\text{C}_6\text{H}_5\text{CH}=\text{CH}-$, E_1 and E_2 both being carbon atoms:

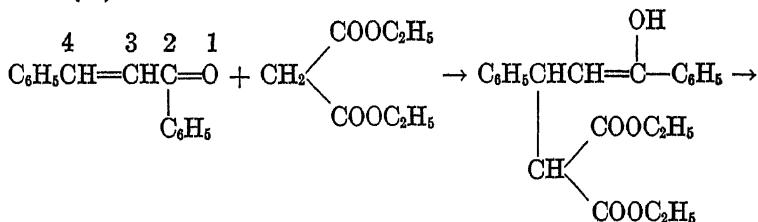


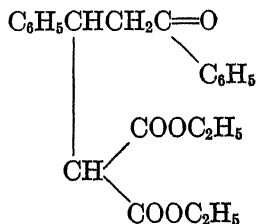
THE ALDOL AND MICHAEL CONDENSATIONS

The condensation reactions of α, β -unsaturated carbonyl compounds may be either of the 1,2 or aldol type, or of the 1,4 or Michael type. Cinnamaldehyde and ethyl cyanoacetate, for example, react in the 1,2 manner (9):



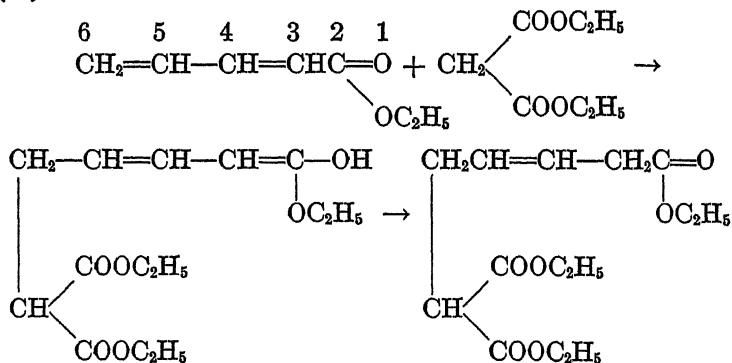
On the other hand, malonic ester adds to benzalacetophenone in the 1,4 fashion (46):



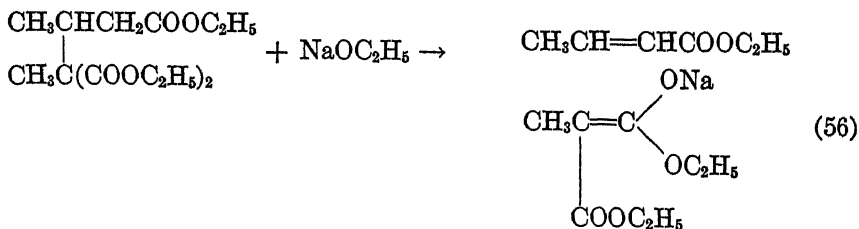
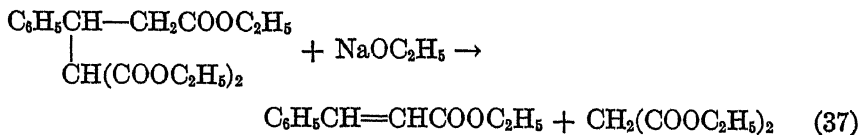


It is evident from these examples that the aldol condensation becomes the Michael condensation when, in the vinylogs of the simple carbonyl compounds, the function of the carbon atom in position 2 is usurped by that in position 4.

The Michael condensation occurs in a 1,6 manner with the next higher vinylog. Thus β -vinylacrylic ester condenses with malonic ester in this way (12):



In view of this close relationship between the aldol and the Michael types of condensation it is interesting to note that the reversibility of the aldol type of reaction is characteristic, likewise, of the Michael condensation. The following are illustrative examples of fissions of this type:

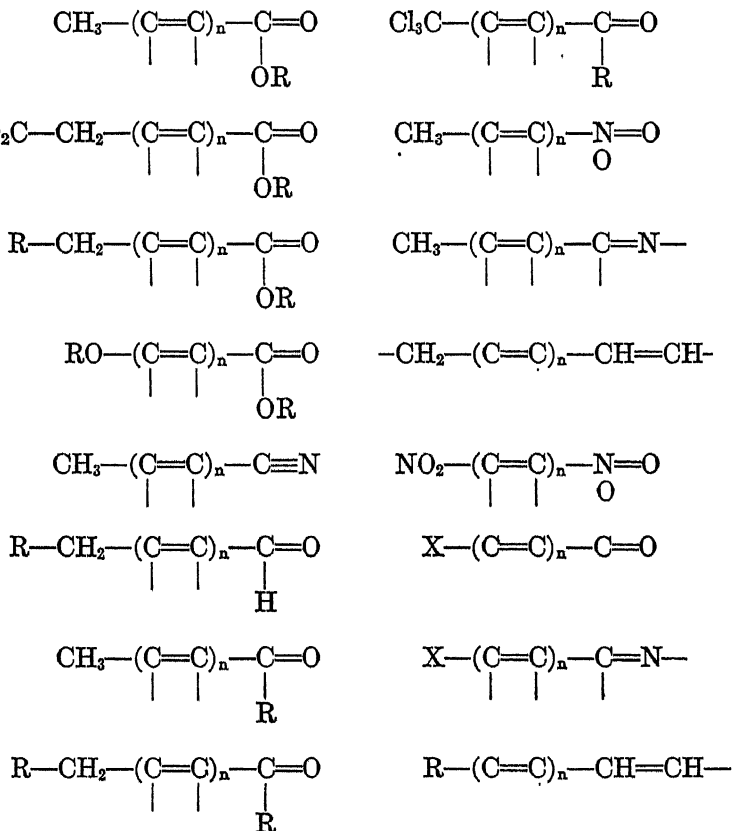


SUMMARY AND DISCUSSION

The principle of vinylogy states that when, in a compound of the type $A-E_1=E_2$ or $A-E_1\equiv E_2$ (in which E_1 and E_2 represent non-metallic elements), a structural unit of the type $-(C=C)_n-$ is interposed between A and E_1 , the function of E_2 remains qualitatively unchanged but that of E_1 may be usurped by the carbon atom attached to A .

The resulting compound has the form $A-(\overset{\textstyle |}{\text{C}}=\overset{\textstyle |}{\text{C}})_n-E_1=E_2$ or $A-(\overset{\textstyle |}{\text{C}}=\overset{\textstyle |}{\text{C}})_n-E_1\equiv E_2$, and in any given series of this type the members differ from each other by one or more vinylene residues. Such a group of compounds has been termed a *vinyllogous series*. The members of such a series are *vinyllogs* of one another.

Examples of the following vinylogous series have been mentioned, and in each case it is shown that the principle of vinylogy is applicable:



It is generally recognized that the behavior of any class of organic compounds represents a resultant of several tendencies, and that usually no one of these tendencies will predominate throughout the whole range of the series. Hence, it is to be expected that any generalization which predicts uniform behavior for all the members of the series will be subject to exceptions. In view of this situation, it is recognized that the principle of vinylogy is not to be regarded as a rule. It states, not that the function of E_1 will be usurped by the carbon atom joined to A, but that it *may* be usurped. Further, it is not implied that effects of the types discussed will not be encountered with structures which lie outside the general category covered by the principle.

The principle of vinology has been used in this review to correlate in a helpful manner many types of reactions which are ordinarily regarded as somewhat anomalous in nature. Also, it is made apparent that this principle may serve to direct attention to possible reactions which might otherwise appear unlikely.

REFERENCES

- (1) ANGELI: Rend. Lincei 8, 2 sem., 32 (1899).
- (2) ANGELI: Mem. accad. Lincei [5] 14, 627 (1924).
- (3) ANGELI: Sammlung Prof. Ahrens, Stuttgart, 28, 1 (1926).
- (4) ANGELI: Atti accad. Lincei [6] 3, 371 (1926).
- (5) ANGELI AND ALESSANDRI: Rend. Lincei 19, 1 sem., 784 (1910).
- (6) BAMBERGER AND BERLÉ: Ann. 273, 303 (1893).
- (7) BARBIER AND BOUVEAULT: Compt. rend. 120, 1420 (1895).
- (8) BARBIER AND BOUVEAULT: Bull. soc. chim. [3] 15, 1008 (1896).
- (9) BECHERT: J. prakt. Chem. [2] 50, 13 (1894).
- (10) BENNETT AND WILLIS: J. Chem. Soc. 1928, 1960.
- (11) BLAISE: Bull. soc. chim. [3] 29, 1015 (1903).
- (12) BLOOM AND INGOLD: J. Chem. Soc. 1931, 2765.
- (13) BOGERT AND FOURMAN: J. Am. Chem. Soc. 55, 4670 (1933).
- (14) BORSCHKE: Ber. 56, 2357 (1923).
- (15) BORSCHKE AND MANTEUFFEL: Ber. 65, 868 (1932).
- (16) BORSCHKE AND MANTEUFFEL: Ann. 512, 97 (1934).
- (17) CLAISEN: Ber. 59, 144 (1926).
- (18) CLAISEN AND HAASE: Ann. 297, 78 (1897).
- (19) DAUTWITZ: Monatsh. 27, 773 (1906).
- (20) DIECKMANN: Ber. 47, 1428 (1914).
- (21) DIECKMANN AND MEISER: Ber. 41, 3259 (1908).
- (22) DIELS AND ALDER: Ber. 62, 2081 (1929).
- (23) DOEBNER AND MILLER: Ber. 18, 1646 (1885).
- (24) ECKERT AND SEIDEL: J. prakt. Chem. 102, 338 (1921).
- (25) FARMER AND MEHTA: J. Chem. Soc. 1931, 2561.
- (26) FARMER AND WARREN: J. Chem. Soc. 1929, 897.
- (27) FICHTER AND SCHWAB: Ann. 348, 251 (1906).
- (28) FLEISCHHAUER: J. prakt. Chem. [2] 47, 376 (1893).
- (29) FRIEDLÄNDER: Ber. 38, 159 (1905).
- (30) FUSON AND ELLINGBOE: Unpublished work.
- (31) GRAEBE AND MARTZ: Ann. 340, 220 (1905).
- (32) HAHN AND WASSMUTH: Ber. 67, 696 (1934).

- (33) HENRICH: *Monatsh.* **20**, 565 (1899); *Ber.* **35**, 1666 (1902).
- (34) HENRY: *Compt. rend.* **120**, 1266 (1895).
- (35) HENZE: *Ber.* **67**, 750 (1934).
- (36) HURTLEY: *J. Chem. Soc.* **1929**, 1870.
- (37) INGOLD AND POWELL: *J. Chem. Soc.* **119**, 1976 (1921).
- (38) JACKSON AND GRINDLEY: *Am. Chem. J.* **17**, 595 (1895).
- (39) JACOBSEN AND REIMER: *Ber.* **16**, 2606 (1883).
- (40) JOHN: *Ber.* **59B**, 722 (1926).
- (41) KATWINKEL AND WOLFFENSTEIN: *Ber.* **37**, 3221 (1904).
- (42) KEKULÉ: *Ann.* **162**, 92 (1872).
- (43) KOENIGS: *Ber.* **25**, 797 (1892).
- (44) KOENIGS: *Ber.* **34**, 4326 (1901).
- (45) KOHLER: *Am. Chem. J.* **31**, 642 (1904).
- (46) KOHLER: *Am. Chem. J.* **46**, 481 (1911).
- (47) KUHN, REINEMUND, AND WEYGAND: *Ber.* **67**, 1460 (1934).
- (48) KUHN AND WAGNER-JAUREGG: *Ber.* **63B**, 2662 (1930).
- (49) KUHN AND WINTERSTEIN: *Helv. Chim. Acta* **11**, 87 (1928).
- (50) LAPWORTH: *Proc. Chem. Soc.* **16**, 132 (1900).
- (51) LAUBENHEIMER: *Ber.* **9**, 1828 (1876).
- (52) LAUBENHEIMER: *Ber.* **11**, 1155 (1878).
- (53) LOBRY DE BRUYN: *Rec. trav. chim.* **9**, 210 (1890).
- (54) LOBRY DE BRUYN: *Rec. trav. chim.* **2**, 236 (1883); **13**, 124 (1894).
- (55) MEERWEIN: *Ann.* **358**, 71 (1908).
- (56) MICHAEL AND ROSS: *J. Am. Chem. Soc.* **52**, 4601 (1930).
- (57) MILLS AND SMITH: *J. Chem. Soc.* **121**, 2724 (1922).
- (58) PFEIFFER AND MONATH: *Ber.* **39**, 1306 (1906).
- (59) POGGI: *Atti della Societa Italiana per il Progresso delle Scienze, XXI Riunione* **2**, 376 (1933).
- (60) PRAGER: *Ann.* **338**, 360 (1905).
- (61) REISSERT: *Ber.* **30**, 1030 (1897).
- (62) REYNOLDS: *Am. Chem. J.* **44**, 305 (1910).
- (63) RÜGHEIMER AND HANKEL: *Ber.* **29**, 2176 (1896).
- (64) RUHEMANN AND WRAGG: *J. Chem. Soc.* **79**, 1190 (1901).
- (65) SACHS AND KEMPF: *Ber.* **35**, 1224 (1902).
- (66) SCHLENK AND BERGMANN: *Ann.* **479**, 64 (1930).
- (67) SCHUSTER: *Ber.* **25**, 2398 (1892).
- (68) SMITH: *J. Am. Chem. Soc.* **56**, 472 (1934).
- (69) SMITH AND DOBROVOLNY: *J. Am. Chem. Soc.* **48**, 1693 (1926).
- (70) THIELE: *Ann.* **306**, 87 (1899).
- (71) THIELE: *Ber.* **32**, 1293 (1899).
- (72) THIELE AND ESCALES: *Ber.* **34**, 2842 (1901).
- (73) TIEMANN AND KRUGER: *Ber.* **26**, 2675 (1893).
- (74) TIEMANN AND KRUGER: *Ber.* **26**, 2693 (1893).
- (75) SEMMLER: *Ber.* **24**, 202 (1891).
- (76) ULLMANN AND ZLOKASOFF: *Ber.* **38**, 2111 (1905).
- (77) WALLACH AND WÜSTEN: *Ber.* **16**, 2008 (1883).
- (78) WISLICENUS: *Ann.* **246**, 315 (1888).
- (79) WISLICENUS AND ELVERT: *Ber.* **42**, 1144 (1909).
- (80) WISLICENUS AND KLEISINGER: *Ber.* **42**, 1140 (1909).
- (81) WISLICENUS AND SCHÖLLKOPF: *J. prakt. Chem.* **95**, 269 (1917).
- (82) WOHL: German patent 116,790; *Chem. Zentr.* **1901**, I, 149.
- (83) ZIEGLER AND CRÖSSMANN: *Ann.* **511**, 89 (1934).

ON THE EXACT SIGNIFICANCE OF THE THERMODYNAMIC QUANTITIES ΔF AND ΔF^0

PIERRE VAN RYSSELBERGHE

Department of Chemistry, Stanford University, California

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It has been customary in recent years to consider the absolute value of ΔF as a measure of the affinity of chemical reactions (3, 4). This ΔF is the finite difference between the free energy in the final state and that in the initial state, these states being separated by one occurrence of the reaction, as written in ordinary chemistry, at constant pressure and temperature. A close theoretical examination of the properties of ΔF and of the various methods used in its determination reveals certain difficulties as to its significance. In particular, what is the exact physical meaning of the so-called standard free energy change ΔF^0 defined by the relation

$$\Delta F^0 = - RT \ln K \quad (1)$$

in which K is the equilibrium constant expressed in terms of mole fractions? The closely related ΔF_1^0 defined by

$$\Delta F_1^0 = - RT \ln K_p \quad (2)$$

in which K_p is the equilibrium constant expressed in terms of partial pressures (in the case of gas reactions) also requires investigation.

Putting aside any discussion of previous writings on the subject, we shall give the exact and general definitions of these two quantities by means of a straightforward thermodynamic reasoning. Let us first indicate the notations and recall certain thermodynamic formulas. We shall present the reasoning in terms of a general chemical reaction

$$0 = \sum_{\gamma''} \nu_{\gamma''} M_{\gamma''} + \sum_{\gamma'} \nu_{\gamma'} M_{\gamma'} \quad (3)$$

The $M_{\gamma''}$'s are the chemical symbols of the components which are usually written on the left-hand side of the chemical reaction. Their coefficients $\nu_{\gamma''}$ are hence negative. The $M_{\gamma'}$'s are the chemical symbols of the components on the right-hand side. Their coefficients $\nu_{\gamma'}$ are positive. The

number of moles of the component γ will be represented by n_γ . The mole fraction of the component γ will be represented by N_γ , with

$$N_\gamma = \frac{n_\gamma}{\sum_\gamma n_\gamma} = \frac{n_\gamma}{n} \quad (4)$$

The chemical potential or partial molar free energy will be called μ_γ . We have (1, 2)

$$\mu_\gamma = \mu_\gamma^0(p, T) + RT \ln N_\gamma f_\gamma \quad (5)$$

μ_γ^0 is a function of pressure and temperature alone and is characteristic of the chemical species γ . f_γ is the activity coefficient. The equilibrium constant $K(p, T)$ is defined by

$$\ln K(p, T) = - \frac{1}{RT} \sum_\gamma \nu_\gamma \mu_\gamma^0(p, T) \quad (6)$$

The degree of advancement of the reaction will be called ξ (1). It is defined by the differential relations

$$\frac{dn_1}{\nu_1} = \frac{dn_2}{\nu_2} = \dots \frac{dn_\gamma}{\nu_\gamma} = \dots d\xi \quad (7)$$

Calling n_γ^0 the number of moles of component γ at time zero, we have

$$n_\gamma = n_\gamma^0 + \nu_\gamma \xi \quad (8)$$

The free energy at any time t is given by

$$F = \sum_\gamma n_\gamma \mu_\gamma \quad (9)$$

or, according to equation 5,

$$F = \sum_\gamma n_\gamma \mu_\gamma^0 + RT \sum_\gamma n_\gamma \ln N_\gamma f_\gamma \quad (10)$$

In the initial state the free energy is given by equation 10 and ξ is assumed to be zero. At the time t the reaction 1 has occurred once and ξ is equal to 1. Temperature and pressure are kept constant and F becomes, according to equations 10, 8, and 4,

$$F + \Delta F = \sum_\gamma (n_\gamma + \nu_\gamma) \mu_\gamma^0 + RT \sum_\gamma (n_\gamma + \nu_\gamma) \ln \frac{n_\gamma + \nu_\gamma}{n + \nu} f'_\gamma \quad (11)$$

in which

$$\nu = \sum_\gamma \nu_\gamma \quad (12)$$

and the f_γ'' 's are the activity coefficients corresponding to the new composition of the system. From equations 11 and 10 we deduce

$$\Delta F = \sum_\gamma \nu_\gamma \mu_\gamma^0 + RT \sum_\gamma \left[(n_\gamma + \nu_\gamma) \ln \frac{n_\gamma + \nu_\gamma}{n + \nu} f'_\gamma - n_\gamma \ln \frac{n_\gamma}{n} f_\gamma \right] \quad (13)$$

or also, according to equation 6,

$$\Delta F = -RT \ln K + RT \ln \prod_\gamma \left(\frac{n_\gamma + \nu_\gamma}{n + \nu} f'_\gamma \right)^{n_\gamma + \nu_\gamma} \cdot \left(\frac{n}{n_\gamma f_\gamma} \right)^{n_\gamma} \quad (14)$$

ΔF is thus obviously a function, not only of the mole fractions n_γ/n , but also of the n_γ 's themselves and hence of the size of the system. Let us examine the behavior of ΔF when, the initial mole fractions being kept constant, the various n_γ 's tend towards infinity. Formula 14 can be written

$$\Delta F = -RT \ln K + RT \ln \prod_\gamma \frac{\left(1 + \frac{\nu_\gamma}{n_\gamma}\right)^{n_\gamma + \nu_\gamma}}{\left(1 + \frac{\nu}{n}\right)^{n_\gamma + \nu_\gamma}} \cdot \left(\frac{n_\gamma}{n}\right)^{\nu_\gamma} \cdot \frac{f_\gamma'^{n_\gamma + \nu_\gamma}}{f_\gamma^{n_\gamma}} \quad (15)$$

or also

$$\Delta F = -RT \ln K + RT \ln \left\{ \frac{\prod_\gamma \left(1 + \frac{1}{\frac{n_\gamma}{\nu_\gamma}}\right)^{n_\gamma}}{\left(1 + \frac{1}{\frac{n}{\nu}}\right)^n} \cdot \prod_\gamma \left(\frac{n_\gamma + \nu_\gamma}{n + \nu}\right)^{\nu_\gamma} \cdot \frac{f_\gamma'^{n_\gamma + \nu_\gamma}}{f_\gamma^{n_\gamma}} \right\} \quad (16)$$

When the various n_γ/ν_γ 's tend towards infinity we have

$$\lim \left(1 + \frac{1}{\frac{n_\gamma}{\nu_\gamma}}\right)^{n_\gamma} = e^{\nu_\gamma} \quad (17.1)$$

$$\lim \left(1 + \frac{1}{\frac{n}{\nu}}\right)^n = e^\nu \quad (17.2)$$

$$\lim \frac{n_\gamma + \nu_\gamma}{n + \nu} = \lim \frac{n_\gamma}{n} = N_\gamma \quad (17.3)$$

and, since initial and final composition become now identical,

$$\lim f'_\gamma = f_\gamma \quad (17.4)$$

From formula 16 we then deduce

$$\lim (\Delta F)_{\text{all } n_\gamma \rightarrow \infty} = -RT \ln K + RT \ln \prod_\gamma (N_\gamma f_\gamma)^{\nu_\gamma} \quad (18)$$

Formula 18 gives the free energy change involved in one occurrence of the reaction in an infinitely large system whose composition is defined by the N_γ 's. We thus see that the standard free energy change

$$\Delta F^0 = -RT \ln K \quad (19)$$

is a particular case of formula 18 corresponding to a composition such that

$$\prod_{\gamma} (N_{\gamma} f_{\gamma})^{\nu_{\gamma}} = 1 \quad (20.1)$$

or

$$\prod_{\gamma'} (N_{\gamma'} f_{\gamma'})^{\nu_{\gamma'}} = \prod_{\gamma''} (N_{\gamma''} f_{\gamma''})^{|\nu_{\gamma''}|} \quad (20.2)$$

This condition expresses that the product of the activities of the various components on the right-hand side of the reaction, taken with their respective exponents $\nu_{\gamma'}$, is equal to the corresponding product for the components on the left-hand side. The particular composition for which this condition is satisfied depends on the type of reaction (coefficients ν_{γ}) and on the relations between the various activity coefficients and composition. It would thus have to be determined for each individual case. Formula 20.1 is of course satisfied when all the activities are equal to unity, but such a state is often physically impossible, as can easily be realized by considering the particular case of ideal or nearly ideal systems. One could make all the activities equal to unity by separating the components in such a way that each one forms an independent phase, but the reaction is then often fictitious, although the ΔF could still be calculated (see below). The main result of this discussion is that ΔF , in order to have the exact meaning implied by its mathematical symbol, must refer to an infinitely large system.

It can easily be verified that ΔF , as given by formula 18, is simply, in absolute value, the *affinity* in De Donder's sense (1). The affinity being

$$\mathcal{A} = - \left(\frac{\partial F}{\partial \xi} \right)_{pT} \quad (21)$$

we deduce from formulas 10 and 7 and from the well-known Gibbs-Duhem formula that

$$-\mathcal{A} = -RT \ln K + RT \ln \prod_{\gamma} (N_{\gamma} f_{\gamma})^{\nu_{\gamma}} \quad (22)$$

$\mathcal{A}$ is an intensive property and does not depend on the size of the system. ΔF is thus actually an affinity (in absolute value) and should be written $\left(\frac{\partial F}{\partial \xi} \right)_{pT}$ or $-\mathcal{A}$.

In the case of gas reactions the rather unfortunate custom of using the equilibrium constant K_p is prevalent. Between K and K_p the following relation holds

$$K_p = Kp^\nu \quad (23)$$

with

$$K_p = \prod_{\gamma} (p_{\gamma} f_{\gamma})^{\nu_{\gamma}} \quad (24)$$

p_{γ} is the partial pressure of component γ , p the total pressure.

We have, in the case of gases

$$p_{\gamma} = N_{\gamma} p \quad (25)$$

From formulas 18 and 23 we easily deduce, for an infinitely large system,

$$\Delta F = -RT \ln K_p + RT \ln p^{\nu} \prod_{\gamma} (N_{\gamma} f_{\gamma})^{\nu_{\gamma}} \quad (26)$$

The standard free energy change

$$\Delta F_1^0 = -RT \ln K_p \quad (27)$$

thus corresponds to a state such that

$$p^{\nu} \prod_{\gamma} (N_{\gamma} f_{\gamma})^{\nu_{\gamma}} = 1 \quad (28)$$

If $\nu = 0$, this condition becomes equivalent to 20.2. If ν is different from 0, formula 28 is satisfied when we have separately

$$p = 1 \quad (29.1)$$

and

$$\prod_{\gamma'} (N_{\gamma'} f_{\gamma'})^{\nu_{\gamma'}} = \prod_{\gamma''} (N_{\gamma''} f_{\gamma''})^{\nu_{\gamma''}} \quad (29.2)$$

or also when all the $p_{\gamma} f_{\gamma}$ defined by formula 25 are equal to unity. Here again ΔF refers to an infinitely large system. One can only dispense with this restriction as to the size of the system by writing $\left(\frac{\partial F}{\partial \xi}\right)_{pT}$ instead of ΔF . Another way of explaining this point is the following: By increasing the size of the system we may have a gradual transition of the type

$$\left(\frac{\partial F}{\partial \xi}\right)_{pT} \longrightarrow \left(\frac{\Delta F}{\Delta \xi}\right)_{pT} \quad (30)$$

meaning that $\left(\frac{\Delta F}{\Delta \xi}\right)_{pT}$ becomes a better approximation for $\left(\frac{\partial F}{\partial \xi}\right)_{pT}$ as the system becomes larger. $\Delta \xi$ can only be considered as infinitesimally small

if the size of the system, i.e., the various n_γ 's, and hence F , are infinitely large. If we now make $\Delta\xi = 1$, formula 30 becomes

$$\left(\frac{\partial F}{\partial \xi}\right)_{pT} = \lim_{n_\gamma \rightarrow \infty} (\Delta F)_{\Delta\xi=1} \quad (31)$$

It is obvious that most thermodynamic reasoning and calculations involving these quantities will be made more exact and more straightforward by using $\left(\frac{\partial F}{\partial \xi}\right)_{pT}$ instead of ΔF .

Analogous conclusions could be obtained concerning other familiar thermodynamic quantities such as ΔU , ΔH , ΔC_p , ΔC_v , etc. For instance, $\left(\frac{\partial H}{\partial \xi}\right)_{pT}$ is equal to the instantaneous heat of reaction at constant pressure and temperature, while ΔH refers to an infinitely large system or, as is often the case in practice, it is the average heat of reaction between two states of a finite system separated by a $\Delta\xi$ equal to 1.

In practice one frequently calculates the free energy change corresponding to one occurrence of the reaction when each reactant is considered as forming an independent phase. The reaction is then often a fictitious one, but the ΔF can be calculated in a direct manner. Let us note that the building up of galvanic cells is a partial realization of this separation into independent phases. If component γ forms a phase by itself, its partial molar free energy is given by

$$\mu_\gamma = \mu_\gamma^0(p, T) \quad (32)$$

obtained by replacing both N_γ and f_γ by unity in formula 5. Let us consider $|\nu_{\gamma''}|$ moles of each component γ'' appearing in the reaction 1, each group of $|\nu_{\gamma''}|$ moles forming a separate phase. The free energy in the initial state is then

$$F_i = - \sum_{\gamma''} \nu_{\gamma''} \mu_{\gamma''}^0(p, T) \quad (33)$$

The reaction is assumed to go to completion and the final state is chosen such that there are $\nu_{\gamma'}$ moles of each component γ' in as many separate phases as there are components of this type. The free energy in the final state is then

$$F_f = \sum_{\gamma'} \nu_{\gamma'} \mu_{\gamma'}^0(p, T) \quad (34)$$

and ΔF is given by

$$\Delta F = F_f - F_i = \sum_{\gamma'} \nu_{\gamma'} \mu_{\gamma'}^0 + \sum_{\gamma''} \nu_{\gamma''} \mu_{\gamma''}^0 = \sum_{\gamma} \nu_{\gamma} \mu_{\gamma}^0 \quad (35)$$

which, according to formula 6, can also be written

$$\Delta F = - RT \ln K \quad (36)$$

We thus see that this ΔF is identical with the standard ΔF^0 studied above, for which a new interpretation is now provided.

If ΔF^0 is determined by means of the relation

$$\Delta F^0 = \Delta H^0 - T\Delta S^0 \quad (37)$$

both ΔH^0 and ΔS^0 should refer to this system of separated phases. The classical method for the calculation of ΔS^0 from the heat capacity data of the pure compounds is in agreement with this requirement. ΔH^0 is usually obtained from a combination of combustion and other thermochemical data and is only an approximation (although often a very good one) to the true ΔH^0 , since the resulting compounds (carbon dioxide and water, for instance) are mixed instead of being in separate phases. The true ΔH^0 and ΔS^0 must be such that

$$\Delta F^0 = \Delta H^0 - T\Delta S^0 = -RT \ln K \quad (38)$$

The latter interpretation of ΔF^0 actually considers this quantity as a particular case of the ΔF given by formula 13, while in the first interpretation it is a particular case of the ΔF given by formula 18. Only in this latter case is ΔF^0 a particular value of a true function of the state of the system.

As we have shown, this function is the affinity $-\left(\frac{\partial F}{\partial \xi}\right)_{p,T}$.

SUMMARY

1. The quantity ΔF is calculated by means of the fundamental thermodynamic formula $F = \sum n_{\gamma} \mu_{\gamma}$.

2. It is shown to be a function of the state of the system (pressure, temperature, and mole fractions) only if the system is infinitely large.

3. The standard $\Delta F^0 = -RT \ln K$ is discussed and its exact definition given.

4. A comparison between ΔF and the partial derivative $\left(\frac{\partial F}{\partial \xi}\right)_{p,T}$ (ξ is the degree of advancement of the reaction) is presented.

REFERENCES

- (1) DE DONDER, TH.: *L'Affinité*, Part I. Gauthier-Villars, Paris (1927).
- (2) GUGGENHEIM, E. A.: *Modern Thermodynamics by the Methods of Willard Gibbs*. Methuen and Co., London (1933).
- (3) LEWIS, G. N., AND RANDALL, M.: *Thermodynamics and the Free Energy of Chemical Substances*. McGraw-Hill Book Co., New York (1923).
- (4) PARKS, G. S., AND HUFFMAN, H. M.: *The Free Energies of Some Organic Compounds*. The Chemical Catalog Co., Inc., New York (1932).

THE FUNDAMENTALS OF CHEMICAL THERMODYNAMICS

PIERRE VAN RYSSELBERGHE

Department of Chemistry, Stanford University, California

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I. INTRODUCTION

In recent years a general and accurate method of chemical thermodynamics has been developed by De Donder (1) and, independently, by Schottky, Ulich, and Wagner (6, 7). De Donder's exposition of the subject is particularly clear and rigorous. Its main feature is the introduction of a function of the state of the system called the *affinity*, closely related to the chemical potentials of Gibbs. The object of chemical thermodynamics is the study of reactions actually taking place in time and of the corresponding changes in the various properties of the system. Classical thermodynamics, as treated by Gibbs (3) and quite recently by Guggenheim (4), is mainly concerned with the study of equilibria and reversible changes. The term "thermostatistics", suggested and actually used by several authors, very properly applies to this type of thermodynamics. Chemical thermodynamics would then simply be called thermodynamics.

Lewis and Randall (5) treat both parts of the subject, but their formal treatment of chemical thermodynamics can be improved upon. A monograph by van Lerberghe (8) is particularly instructive from this point of view.

As no attention seems to have been paid so far to this method of thermodynamics in the English or American literature, this introduction to the subject is presented as a service to physical chemists.

II. THE FIRST AND THE SECOND LAW OF THERMODYNAMICS; THERMODYNAMIC FUNCTIONS

The first law of thermodynamics is the principle of the conservation of energy. Let us consider an infinitesimally small transformation of a closed system taking place between the time t and the time $t + dt$ (dt is positive). During this transformation the system receives the quantity of heat¹ dQ , undergoes the exterior work dW , and increases its internal

¹ dQ may or may not be an exact differential. It is the principal part of the increment ΔQ when this increment tends toward zero. We have, for a given transformation of the system:

$$\lim \Delta Q = dQ + \frac{d^2Q}{2!} + \frac{d^3Q}{3!} + \dots$$

d^2Q , d^3Q , etc., are neglected.

energy by the amount dU . The conservation of energy requires that:

$$dQ + dW = dU \quad (2.1)$$

We shall only consider systems for which

$$dW = -pdV \quad (2.2)$$

p being the pressure and V the volume of the system. For the sake of simplicity we shall suppose that temperature and pressure are the same throughout the system. Equation 2.1 becomes:

$$dU = dQ - pdV \quad (2.3)$$

The second law of thermodynamics is the so-called principle of the degradation of energy. It can be made to assume a general mathematical form, thanks to the introduction of the function of the state of the system called entropy. Calling S the entropy and T the absolute temperature of the system, we have for reversible transformations taking place between the times t and $t + dt$ ($dt > 0$)

$$TdS - dQ = 0 \quad (2.4)$$

for irreversible transformations:

$$TdS - dQ > 0 \quad (2.5)$$

Hence the difference $TdS - dQ$ is always positive or equal to zero; it can never be negative for a natural process. This quantity was called by Clausius the uncompensated heat of the process. We shall represent it by the symbol dQ' . We have then according to equation 2.5:

$$TdS = dQ + dQ' \quad (2.6)$$

According to equation 2.4 we have for reversible changes:

$$dQ' = 0 \quad (2.7)$$

and according to equation 2.5 for irreversible changes:

$$dQ' > 0 \quad (2.8)$$

The first law (equation 2.3) can then be written for reversible changes:

$$dU = TdS - pdV \quad (2.9)$$

for irreversible changes:

$$dU = TdS - pdV - dQ' \quad (2.10)$$

Let us now introduce the other thermodynamic functions: the heat content

$$H \equiv U + pV \quad (2.11)$$

the maximum work or free energy of Helmholtz

$$A \equiv U - TS \quad (2.12)$$

the thermodynamic potential of Gibbs or free energy of Gibbs

$$F \equiv U - TS + pV \quad (2.13)$$

From relations 2.10, 2.11, 2.12, and 2.13, we obtain

$$dH = TdS + Vdp - dQ' \quad (2.14)$$

$$dA = -SdT - pdV - dQ' \quad (2.15)$$

$$dF = -SdT + Vdp - dQ' \quad (2.16)$$

We are now able to deduce the following conclusions:

- (1) For a natural process taking place at constant entropy and volume

$$dQ' = -dU > 0 \quad (2.17)$$

- (2) For a natural process taking place at constant entropy and pressure

$$dQ' = -dH > 0 \quad (2.18)$$

- (3) For a natural process taking place at constant temperature and volume

$$dQ' = -dA > 0 \quad (2.19)$$

- (4) For a natural process taking place at constant temperature and pressure

$$dQ' = -dF > 0 \quad (2.20)$$

The relations 2.1 to 2.20 apply to all types of physicochemical changes and constitute the basis of chemical thermodynamics.

III. CRITIQUE OF CURRENT CHEMICAL THERMODYNAMICS

The variation in free energy corresponding to one occurrence of a given chemical reaction at constant temperature and pressure is considered to be a measure of the *affinity* of that reaction. This variation of free energy is represented by ΔF . Relation 2.20 becomes

$$\Delta Q' = -\Delta F > 0 \quad (3.1)$$

which shows that the ΔF of a spontaneous reaction is negative. The composition of the system changing gradually from the initial to the final state, F and hence ΔF are functions of p , T , and the composition. In practice, however, one considers the ΔF corresponding to one complete occurrence of the reaction, the initial state being such that only the components on the left-hand side of the chemical reaction are present.

Various devices are used for the experimental determination and the calculation of ΔF . For instance:

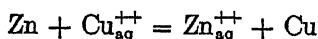
(1) The reaction is made to occur reversibly by means of a separation of the phases of the system and the adjunction of an auxiliary system able to develop a difference of electric potential equal and of opposite sign to that of the chemical system. The complete system is in equilibrium and one writes:

$$\Delta F_{\text{total}} = \Delta F_{\text{reaction}} + NFE = 0 \quad (3.2)$$

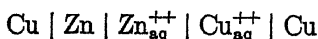
and hence:

$$\Delta F_{\text{reaction}} = - NFE \quad (3.3)$$

(N = number of equivalents involved in one occurrence of the reaction, F = Faraday's constant, and E = electromotive force.) A large number of chemical changes are amenable to this method, but the approximations involved and the limitations of the procedure are usually not fully realized. A moment of thought, however, will easily convince the reader that only for systems containing one reactant per phase does this procedure lead to a good approximation for ΔF . Whenever two or more reactants belong to the same phase and have thus to be separated by means of a membrane or a liquid junction, the measured E.M.F. does not take into account the specific effects of one component upon the thermodynamic properties of the others. The affinity of the reaction



for instance, is deduced from the E.M.F. of a cell of the type:



in which the specific effects resulting from the mixture of the two metallic ions are absent.

(2) The value of ΔF corresponding to a certain mixture of the reactants in which they all possess unit activity is deduced from an equilibrium measurement, at the pressure and temperature desired, by means of the formula

$$\Delta F = - RT \cdot \log K(p, T) \quad (3.4)$$

in which K is the equilibrium constant and R the gas constant.

The composition of the particular mixture corresponding to this ΔF can only be approximated, and there is no way of deducing the value of ΔF for some other composition of the system.

(3) ΔF is often deduced from the relation:

$$\Delta F = \Delta H - T \cdot \Delta S \quad (3.5)$$

in which the three Δ 's correspond to changes taking place at constant temperature. In using actual thermochemical and heat capacity data one has moreover to assume that volume or pressure is constant. Since only the ΔF corresponding to a change at constant temperature and pressure is a measure of the affinity, the ΔH in relation 3.5 is the heat of reaction at constant temperature and pressure and the ΔS is deduced from heat capacities at constant pressure. The dependence of ΔF on composition could only be obtained if the heat of reaction and the entropy were known functions of composition. The present analysis shows the absolute necessity of introducing a "chemical variable" to complete the definition of the state of the system. This chemical variable will be a measure of the degree of advancement of the reaction; in case several independent reactions occur simultaneously there will be as many chemical variables as reactions. The introduction of such variables is the object of the following section, and we shall therefore interrupt at this point our discussion of current chemical thermodynamics.

IV. THE CHEMICAL VARIABLE

The law of definite proportions

Let us first consider a change of state and take as an example the evaporation of liquid water. The phenomenon can be represented by the "reaction":



The system consists of a liquid phase and a vapor phase and is closed. If m_l is the mass of the liquid and m_v is that of the vapor, we have:

$$dm_l = - dm_v \quad (4.2)$$

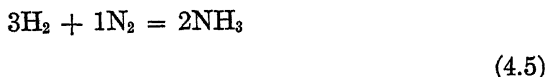
If evaporation is actually taking place, reaction 4.1 goes from left to right, dm_l is negative, and dm_v is positive. The number of moles of water evaporated is given by:

$$-\frac{dm_l}{M_{\text{H}_2\text{O}}} = \frac{dm_v}{M_{\text{H}_2\text{O}}} = d\xi \quad (4.3)$$

$M_{\text{H}_2\text{O}}$ being the molecular mass of water. ξ is a pure number. It can be considered as the "degree of advancement" of the process.² If we write equation 4.1 as follows:

$$0 = -1(\text{H}_2\text{O})_{\text{liquid}} + 1(\text{H}_2\text{O})_{\text{vapor}} \quad (4.4)$$

we see that the signs of the ratios appearing in equation 4.3 are given by the signs of the coefficients of the chemical symbols in equation 4.4. Let us now take the case of a typical chemical reaction, the formation of ammonia from hydrogen and nitrogen. The chemical reaction is:



or

$$0 = -3\text{H}_2 - 1\text{N}_2 + 2\text{NH}_3$$

The masses of hydrogen and nitrogen are decreasing; that of ammonia is increasing, and by analogy with equation 4.3 we have:

$$\frac{dm_{\text{H}_2}}{-3M_{\text{H}_2}} = \frac{dm_{\text{N}_2}}{-1M_{\text{N}_2}} = \frac{dm_{\text{NH}_3}}{+2M_{\text{NH}_3}} = d\xi \quad (4.6)$$

Equation 4.6 is the mathematical form of the law of definite proportions. ξ is the degree of advancement of the reaction. It gives the number of molar groups formed (2NH_3) or destroyed (3H_2 , 1N_2) during the reaction.

If at the beginning (time zero) the mass of ammonia is zero, we have at time t , when ξ molar groups have been formed:

$$\begin{aligned} m_{\text{NH}_3} &= 2M_{\text{NH}_3} \cdot \xi \\ m_{\text{H}_2} &= m_{\text{H}_2}^0 - 3M_{\text{H}_2} \cdot \xi \\ m_{\text{N}_2} &= m_{\text{N}_2}^0 - M_{\text{N}_2} \cdot \xi \end{aligned} \quad (4.7)$$

$m_{\text{H}_2}^0$ and $m_{\text{N}_2}^0$ are the masses of hydrogen and nitrogen at the time zero. These relations are immediately obtained by integration of the differential equations 4.6.

It is now easy to generalize. In the case of a single reaction we may write

$$\sum_{\gamma''} |\nu_{\gamma''}| \cdot \bar{M}_{\gamma''} = \sum_{\gamma'} \nu_{\gamma'} \bar{M}_{\gamma'} \quad (4.8)$$

$|\nu_{\gamma''}|$ is the absolute value of the coefficient of the chemical symbol $M_{\gamma''}$ of the constituent γ'' whose mass decreases in the process (reaction from left

² In French: *degré d'avancement* (cf. De Donder). In German: *Reaktionslaufzahl* (cf. Schottky).

to right). $\nu_{\gamma''}$ is actually negative. $\nu_{\gamma''}$ is the coefficient of the chemical symbol $\bar{M}_{\gamma'}$ of the constituent γ' whose mass increases in the process. $\nu_{\gamma'}$ is positive. Equation 4.8 can also be written:

$$0 = \sum_{\gamma=1}^{\gamma=c} \nu_{\gamma} \bar{M}_{\gamma} \quad (4.9)$$

in which the summation is extended to all the constituents, whether on the left or the right of equation 4.8. The ν_{γ} 's of the constituents on the left are negative, those of the constituents on the right are positive. By analogy with equations 4.3 and 4.6 we write:

$$\frac{dm_{\gamma}}{\nu_{\gamma} \bar{M}_{\gamma}} = d\xi \quad (4.10)$$

for $\gamma = 1, 2, \dots, c$. The ν_{γ} 's are again taken with their signs.

In the case of a system of φ phases ($a = 1, 2, \dots, \varphi$) in which one reaction takes place, equation 4.10 becomes

$$\sum_a \frac{dm_{\gamma a}}{\nu_{\gamma} \bar{M}_{\gamma}} = d\xi \quad (4.11)$$

In the case of a system of one phase in which r independent reactions take place ($\rho = 1, 2, \dots, r$), equation 4.10 becomes

$$\frac{dm_{\gamma \rho}}{\nu_{\gamma \rho} \bar{M}_{\gamma}} = d\xi_{\rho} \quad (4.12)$$

Finally, in the case of a system of φ phases in which r independent reactions take place, equation 4.10 becomes

$$\sum_a \frac{dm_{\gamma a \rho}}{\nu_{\gamma \rho} \bar{M}_{\gamma}} = d\xi_{\rho} \quad (4.13)$$

By independent reactions we mean reactions such that none can be obtained by means of a linear combination of two or more of the others.

Introducing the numbers of moles

$$dn_{\gamma} = \frac{dm_{\gamma}}{\bar{M}_{\gamma}} \quad (4.14)$$

the general expression 4.13 becomes

$$\sum_a \frac{dn_{\gamma a \rho}}{\nu_{\gamma \rho}} = d\xi_{\rho} \quad (4.15)$$

from which one easily deduces that

$$dn_\gamma = \sum_\rho \nu_{\gamma\rho} d\xi_\rho \quad (4.16)$$

and also that

$$dn_\gamma = \sum_\rho \sum_a dn_{\gamma a \rho} \quad (4.17)$$

The velocity of the reaction ρ is conveniently defined as follows:

$$v_\rho = \frac{d\xi_\rho}{dt} = \frac{1}{\nu_\gamma} \cdot \frac{dn_\gamma}{dt} \quad (4.18)$$

Let us emphasize that in a closed system in which chemical reactions are taking place the dn_γ 's are not independent. They are connected by the law of definite proportions with the degrees of advancement of the independent reactions. These degrees of advancement are independent variables and play in chemical thermodynamics a part entirely analogous to that of pressure and temperature, for instance.

V. DEFINITION OF AFFINITY; FUNDAMENTAL HYPOTHESIS

In this section we shall develop a line of reasoning which could be based upon any one of the four equations 2.10, 2.14, 2.15, and 2.16. Let us, for instance, use equation 2.16:

$$dF = -SdT + Vdp - dQ' \quad (5.1)$$

We easily see that F should be considered as a function of T , p , and composition. Let us assume, for the sake of simplicity, that only one reaction occurs in the system. F is then a function of T , p , and ξ :

$$F = F(p, T, \xi) \quad (5.2)$$

We should have

$$dQ' = a_{p\xi} \cdot dT + a_{T\xi} \cdot dp + a_{pT} \cdot d\xi \quad (5.3)$$

in which $a_{p\xi}$, $a_{T\xi}$, and a_{pT} are also functions of p , T , and ξ . Equation 5.1 becomes

$$dF = -(S + a_{p\xi}) dT + (V - a_{T\xi}) dp - a_{pT} d\xi \quad (5.4)$$

During the reaction the variables p , T , and ξ are functions of time only:

$$\left. \begin{aligned} p &= p(t) \\ T &= T(t) \\ \xi &= \xi(t) \end{aligned} \right\} \quad (5.5)$$

Eliminating t we may write:

$$\left. \begin{aligned} p &= p(\xi) \\ T &= T(\xi) \end{aligned} \right\} \quad (5.6)$$

from which the derivatives $\frac{dp}{d\xi}$ and $\frac{dT}{d\xi}$ can be calculated. Equation 5.3 may be written:

$$\frac{dQ'}{d\xi} = a_{p\xi} \cdot \frac{dT}{d\xi} + a_{T\xi} \cdot \frac{dp}{d\xi} + a_{pT} \quad (5.7)$$

and 5.4:

$$\frac{dF}{d\xi} = - (S + a_{p\xi}) \frac{dT}{d\xi} + (V - a_{T\xi}) \frac{dp}{d\xi} - a_{pT} \quad (5.8)$$

For the particular case of a reaction taking place at constant p and T , equations 5.7 and 5.8 become, respectively,

$$\left(\frac{dQ'}{d\xi} \right)_{pT} = a_{pT} \quad (5.9)$$

and

$$\left(\frac{dF}{d\xi} \right)_{pT} = - a_{pT} \quad (5.16)$$

We shall now introduce a fundamental hypothesis entirely in agreement with the accepted methods of thermodynamics which indeed implicitly apply it. This hypothesis was first clearly stated by De Donder (1): $\frac{dQ'}{d\xi}$ is always equal to a_{pT} whatever the manner in which p and T depend on ξ may be, i.e., whatever the relations 5.6 may be. In other words we must have:

$$\frac{dQ'}{d\xi} = a_{p\xi} \frac{dT}{d\xi} + a_{T\xi} \frac{dp}{d\xi} + a_{pT} \equiv a_{pT} \quad (5.11)$$

for all values of $\frac{dT}{d\xi}$ and $\frac{dp}{d\xi}$. Hence the necessary conditions

$$a_{p\xi} = a_{T\xi} = 0 \quad (5.12)$$

The formulas 5.7 and 5.8 become

$$\frac{dQ'}{d\xi} = a_{pT} \quad (5.13)$$

$$dF = - SdT + Vdp - a_{pT}d\xi \quad (5.14)$$

In particular:

$$\left(\frac{\partial F}{\partial \xi}\right)_{pT} = -a_{pT} \quad (5.15)$$

Let us show that equation 5.13 is independent of the choice of variables. If, for instance, we take V , T , ξ instead of p , T , ξ , equation 5.11 becomes

$$\begin{aligned} \frac{dQ'}{d\xi} = & \left[a_{p\xi} + a_{T\xi} \cdot \left(\frac{\partial p}{\partial T}\right)_{V\xi} \right] \frac{dT}{d\xi} \\ & + a_{T\xi} \cdot \left(\frac{\partial p}{\partial V}\right)_{T\xi} \cdot \frac{dV}{d\xi} + a_{pT} + a_{T\xi} \cdot \left(\frac{\partial p}{\partial \xi}\right)_{VT} \end{aligned} \quad (5.16)$$

which, according to equation 5.12, reduces to equation 5.13 whatever $\frac{dT}{d\xi}$ and $\frac{dV}{d\xi}$ may be. We could have started our reasoning with the other thermodynamic functions and we would have found that

$$\frac{dQ'}{d\xi} = a_{SV} = a_{Sp} = a_{VT} = a_{pT} = \mathcal{A} \quad (5.17)$$

The quantity $\mathcal{A}$ is independent of the type of transformation undergone by the system, i.e., it does not depend on the particular way in which the variables S , V , T , or p depend on ξ . It is a function of the state of the system like U , H , A , or F . This function $\mathcal{A}$ was called by De Donder the *affinity* of the system.

Corollary: In the case of transformations such that ξ is constant, i.e., transformations in which the masses of all the constituents in all the phases stay constant (purely physical transformations), we have, according to equation 5.17,

$$dQ' = \mathcal{A}d\xi = 0 \quad (5.18)$$

Hence these transformations are reversible.

From equations 2.10, 2.14, 2.15, 2.16, and 5.17 we deduce the important relations

$$\left(\frac{\partial U}{\partial \xi}\right)_{SV} = \left(\frac{\partial H}{\partial \xi}\right)_{Sp} = \left(\frac{\partial A}{\partial \xi}\right)_{VT} = \left(\frac{\partial F}{\partial \xi}\right)_{pT} = -\mathcal{A} \quad (5.19)$$

We also have

$$\left(\frac{\partial U}{\partial S}\right)_{v\xi} = T \quad (5.20.1) \qquad \left(\frac{\partial U}{\partial V}\right)_{s\xi} = -p \quad (5.20.2)$$

$$\left(\frac{\partial H}{\partial S}\right)_{p\xi} = T \quad (5.20.3) \qquad \left(\frac{\partial H}{\partial p}\right)_{s\xi} = V \quad (5.20.4)$$

$$\left(\frac{\partial A}{\partial T}\right)_{v\xi} = -S \quad (5.20.5) \qquad \left(\frac{\partial A}{\partial V}\right)_{T\xi} = -p \quad (5.20.6)$$

$$\left(\frac{\partial F}{\partial T}\right)_{p\xi} = -S \quad (5.20.7) \qquad \left(\frac{\partial F}{\partial p}\right)_{T\xi} = V \quad (5.20.8)$$

and

$$\begin{aligned} dU &= TdS - pdV - \mathcal{A}d\xi & (5.2) \\ dH &= TdS + Vdp - \mathcal{A}d\xi & (5.2) \\ dA &= -SdT - pdV - \mathcal{A}d\xi & (5.2) \\ dF &= -SdT + Vdp - \mathcal{A}d\xi & (5.2) \end{aligned}$$

It is important to point out that this quantity $\mathcal{A}$ has all the properties usually associated in a qualitative manner with the name "affinity." Since dQ' is always positive and at least equal to zero we have

$$dQ' = \mathcal{A}d\xi \geq 0 \quad (5.25)$$

1. When $\mathcal{A}$ is positive, $d\xi$ is also positive and the process represented by the general reaction 4.8 actually takes place from left to right.

2. When $\mathcal{A}$ is negative, $d\xi$ is also negative and the process represented by equation 4.8 takes place from right to left. The reaction from left to right is impossible.

3. If $\mathcal{A}$ is equal to zero, $d\xi$ may be positive or negative or equal to zero. The system is indifferent with respect to the reaction 4.8.

When ξ stays constant we have, of course,

$$\mathcal{A}d\xi = 0 \quad (5.26)$$

and $\mathcal{A}$ may be different from or equal to zero. When $\mathcal{A}$ is equal to zero and ξ is constant the system is said to be in a state of *true equilibrium*. When $\mathcal{A}$ is different from zero and ξ is constant the system is said to be in a state of *false equilibrium*. The notion of false equilibrium was first introduced by Duhem (2).

VI. RELATION BETWEEN THE AFFINITY AND THE CHEMICAL POTENTIALS

The usual form of the formulas 2.10, 2.14, 2.15, and 2.16 is that due to Gibbs:

$$dU = TdS - pdV + \sum_{\gamma} \sum_a \mu_{\gamma a} dn_{\gamma a} \quad (6.1)$$

$$dH = TdS + Vdp + \sum_{\gamma} \sum_a \mu_{\gamma a} dn_{\gamma a} \quad (6.2)$$

$$dA = -SdT - pdV + \sum_{\gamma} \sum_a \mu_{\gamma a} dn_{\gamma a} \quad (6.3)$$

$$dF = -SdT + Vdp + \sum_{\gamma} \sum_a \mu_{\gamma a} dn_{\gamma a} \quad (6.4)$$

in which $\mu_{\gamma a}$ is the chemical potential of the constituent γ in the phase a . These relations are usually meant to apply to reversible changes, i.e., changes such that $dQ' = 0$. Comparing, for instance, equation 6.4 with equation 5.24, and making use of equation 5.18 we obtain the general condition for equilibrium:

$$dQ' = \mathcal{A}d\xi = - \sum_{\gamma} \sum_a \mu_{\gamma a} dn_{\gamma a} = 0 \quad (6.5)$$

We obviously have

$$\mu_{\gamma 1} = \mu_{\gamma 2} = \dots = \mu_{\gamma \varphi} \quad (6.6)$$

Equation 6.5 becomes then:

$$\mathcal{A}d\xi = - \sum_{\gamma} \mu_{\gamma} \sum_a dn_{\gamma a} = 0 \quad (6.7)$$

but, according to equation 4.15,

$$\sum_a dn_{\gamma a} = \nu_{\gamma} \cdot d\xi \quad (6.8)$$

Hence the condition of equilibrium:

$$\mathcal{A} = - \sum_{\gamma} \nu_{\gamma} \mu_{\gamma} = 0 \quad (6.9)$$

The various formulas of the previous sections apply to irreversible changes. We thus have in general:

$$\mathcal{A}d\xi = - \sum_{\gamma} \sum_a \mu_{\gamma a} dn_{\gamma a} \quad (6.10)$$

The fact that $\mathcal{A}$ and the $\mu_{\gamma a}$'s are here assumed to be defined for states of non-equilibrium should cause no surprise, since such quantities as ΔF , ΔH , ΔS , etc., of current thermodynamics are measured or calculated for irreversible changes. Indeed the method of deducing ΔF from electromotive

force measurements implies the existence of definite chemical potentials for states of non-equilibrium.

For the particular case where there is only one $dn_{\gamma a}$ for each reactant, i.e., when the variation of the total number of moles of the component γ takes place in only one of the phases, formula 6.10 could be written:

$$\mathcal{A} = - \sum_{\gamma} \mu_{\gamma(a)} \cdot \frac{dn_{\gamma(a)}}{d\xi} = - \sum_{\gamma} \mu_{\gamma(a)} \cdot \nu_{\gamma} \quad (6.11)$$

In the case of systems consisting of only one phase, we always have:

$$\mathcal{A} = - \sum_{\gamma} \mu_{\gamma} \nu_{\gamma} \quad (6.12)$$

When several independent reactions take place simultaneously formula 6.10 becomes:

$$\sum_{\rho} \mathcal{A}_{\rho} d\xi_{\rho} = - \sum_{\gamma} \sum_a \mu_{\gamma a} dn_{\gamma a} \quad (6.13)$$

VII. COMPARISON WITH CURRENT CHEMICAL THERMODYNAMICS

In this section we shall review some of the fundamental relations of thermodynamics as commonly used and show how they are modified in the present theory. ΔF at constant temperature and pressure becomes

$$\Delta F \rightarrow \left(\frac{\partial F}{\partial \xi} \right)_{pT} = - \mathcal{A} \quad (7.1)$$

ΔH is usually the ΔH that satisfies the relation:

$$\Delta F = \Delta H - T \Delta S \quad (7.2)$$

valid for processes taking place at constant temperature. It should be written:

$$\left(\frac{\partial F}{\partial \xi} \right)_{pT} = \left(\frac{\partial H}{\partial \xi} \right)_{pT} - T \left(\frac{\partial S}{\partial \xi} \right)_{pT} \quad (7.3)$$

$\left(\frac{\partial H}{\partial \xi} \right)_{pT}$ is the heat of reaction at constant temperature and pressure. We shall represent it by $-z_{pT}$. According to formulas 7.1 and 7.3 we have:

$$\mathcal{A} = z_{pT} + T \left(\frac{\partial S}{\partial \xi} \right)_{pT} \quad (7.4)$$

which is one of the exact forms of Berthelot's principle: the affinity is in general different from the heat of reaction but the difference decreases with temperature and vanishes at the absolute zero.

Kirchhoff's formula

$$\left(\frac{\partial \Delta H}{\partial T} \right)_p = \Delta C_p \quad (7.5)$$

in which ΔC_p is the sum of the heat capacities of the products less the corresponding sum for the reagents, assumes the elegant and accurate form:

$$\left(\frac{\partial z_{pT}}{\partial T}\right)_{p\xi} = - \sum_{\gamma} \nu_{\gamma} C_{p\gamma} \quad (7.6)$$

in which $C_{p\gamma}$ is the partial molar heat capacity of the constituent γ at constant p .

The Gibbs-Helmholtz formula

$$\Delta F - T \left(\frac{\partial \Delta F}{\partial T} \right)_p = \Delta H \quad (7.7)$$

becomes

$$F - T \left(\frac{\partial F}{\partial T} \right)_{p\xi} = H \quad (7.8)$$

or also

$$\left(\frac{\partial \left(\frac{F}{T} \right)}{\partial T} \right)_{p\xi} = - \frac{H}{T^2} \quad (7.9)$$

Formula 7.7 may also be written

$$\left(\frac{\partial F}{\partial \xi} \right)_{pT} - T \left(\frac{\partial^2 F}{\partial T \partial \xi} \right)_p = - z_{pT} \quad (7.10)$$

which, according to formula 7.1, is equivalent to

$$z_{pT} + T^2 \left[\frac{\partial}{\partial T} \left(\frac{A}{T} \right) \right]_{p\xi} = 0 \quad (7.11)$$

a formula which De Donder called Kelvin's formula. This list of formulas could be considerably extended. We shall limit ourselves to the foregoing examples, reserving for other communications the theory of the shifts of equilibrium and of the perturbations of chemical systems, a field in which this method is particularly powerful and yields results of great compactness and elegance. The method has been used in connection with several other fundamental problems for which formal solutions will be found in De Donder's monographs.

SUMMARY

The fundamental laws and formulas of chemical thermodynamics are given an exact and general form, thanks to the systematic use of a new variable called the degree of advancement of the reaction. A function of

the state of the system called the affinity is introduced, and its properties are studied according to De Donder's method.

Current chemical thermodynamics is critically reviewed from this point of view.

REFERENCES

- (1) DE DONDER, TH.: *L'Affinité*. Part I, 1927; Part II, 1931; Part III, 1934. Gauthier-Villars, Paris.
- (2) DUHEM, P.: *Mécanique Chimique*. Hermann, Paris (1897).
- (3) GIBBS, J. W.: *Equilibrium of Heterogeneous Substances*. The Collected Works of Willard Gibbs, Vol. I. Longmans, Green and Co., New York (1928).
- (4) GUGGENHEIM, E. A.: *Modern Thermodynamics by the Methods of Willard Gibbs*. Methuen and Co., London (1933).
- (5) LEWIS, G. N., AND RANDALL, M.: *Thermodynamics and the Free Energy of Chemical Substances*. McGraw-Hill Book Co., New York (1923).
- (6) SCHOTTKY, W., ULICH, H., AND WAGNER, C.: *Thermodynamik*. Springer, Berlin (1929).
- (7) ULICH, H.: *Chemische Thermodynamik*. Steinkopff, Dresden (1930).
- (8) VAN LERBERGHE, G.: *Calcul des Affinités Physico-Chimiques*. Gauthier-Villars, Paris (1931).

A SYMPOSIUM ON INDICATORS¹

INTRODUCTION: A BRIEF HISTORICAL SKETCH

C. J. BROCKMAN

Department of Chemistry, University of Georgia, Athens, Georgia

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As an introduction to this Symposium a very short historical sketch of the developments in the uses of indicators will be of interest. The first reference to the use of a color indicator, as we know it today, is in the work of Robert Boyle, who in 1660 wrote a treatise entitled "The Experimental History of Colours." He used a tincture of *Lignum Nephriticum* (2): "I drop into the infusion just as much distilled vinegar, or other acid liquor as will serve to deprive it of its blueness (which a few drops, if the sour liquid be strong, and the phial small, will suffice to do;), then without changing my posture, I drop and shake into the same phial a small portion of spirit of hartshorn or urine, and finding that upon this affusion the tincture immediately recovers its ceruleous color, ... And therefore I allow myself to guess at the strength of the liquors examined by this experiment, by the quantity of them which is sufficient to destroy or restore the ceruleous colour of our tincture."

Another quotation is interesting (3): "Take good syrup of violets, impregnated with the tincture of the flowers, drop a little of it upon a white paper (for by that means the change of colour will be more conspicuous, and the experiment may be practiced in smaller quantities), and on this liquor let fall two or three drops of spirit either of salt or vinegar, or almost any other eminently acid liquor, and upon the mixture of these you shall find the syrup immediately turned red: . . . if instead of spirit of salt, or that of vinegar, you drop upon the syrup of violets a little oil of tartar per deliquium, or the like quantity of a solution of potashes, and rub them together with your finger, you shall find the blue colour of the syrup turned in a moment into a perfect green."

Besides those already mentioned, Boyle used many other color indicators, among which were: the juice of the blue corn flower (Exp. XXI), coch-

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ineal (Exp. XXIV), turnesol (Exp. XXXVI), infusion of Brazil Wood and Madder (Exp. XXXVII), logwood extract (Exp. XXXIX), turmeric (Exp. XLIX).

It is interesting that Frederic Hoffman considered mineral spirit (carbonic acid) to possess the nature of an acid because when dissolved in water it reddened tincture of turnesol (11).

Almost a century later the *Encyclopedie Methodique, Chimie et Metallurgie*, which was edited by M. Fourcroy at Paris in 1804, stated (7): "Vegetable colours are employed especially for distinguishing between acids and bases. The former redden, or change into a red, some vegetable colours, and one chooses for this purpose the aqueous sugary tincture of violets, or syrup of violets, or tincture of tournesol. The former is reddened only by the strong acids; the second, less blue at the start and tending toward violet, is changed to red by even the most weak acids; so these two coloured reagents are used in this manner as a means of measuring the energy of various acids. Towards alkalis these vegetable colours react differently and are employed for detecting the presence, the energy, concentration and quantity of alkali. In general, alkalis change the blue vegetable colours to green, especially in the case of violets, mauve, carnations, roses, bark of turnips and radishes. Curcuma is very much more sensitive to alkali than the other colours and indicates alkali in quantities which cannot be detected by other means."

A few years later Faraday (8) devotes an entire chapter to "Coloured Tests—Neutralization," in which he gives an intimate discussion of the production and uses of test solutions and test papers in the laboratory and suggests that all work should be done in the "daylight; artificial light not permitting that just estimation of the changes by which the presence of a small amount of acid or alkali is to be determined."

Following the work of Arrhenius (1887) came the concept of acidity resolved into two components, one of which is "normality," which, in the older sense, is the *quantity* factor of "acidity," while the other is the hydrogen-ion concentration, which is the *intensity* factor. In 1909 Sørensen (13) introduced the present mode of expressing hydrogen-ion concentration, namely, pH.

The study of oxidation-reduction indicators is a recent development, at least from the theoretical point of view. It is true that dyes of certain types were used as far back as the time of Pasteur (12), and even the time of Helmholtz (14), to indicate the exhaustion of oxygen from the bacterial culture media which they were using. However, it was not until 1920, when Gillespie (9) published some data on the electrode potentials which were induced by bacterial reduction, that the quantitative study of such oxidation-reduction systems began. Unfortunately, or perhaps fortunately, these

electrode potentials were in some cases uncertain. All of this led finally, in the hands of W. Mansfield Clark, to the development of a supplementary method which could be used to check the electrode measurements of oxidation-reduction intensity. This was the color indicator method, which is to oxidation-reduction systems what the acid-base indicators are in the study of hydrogen-ion equilibria.

W. Mansfield Clark (4) in 1920 reported on the system methylene blue-methylene white. He has now carried his investigations through some twenty papers on the development of color indicators for the study of oxidation-reduction systems in organic reactions. Today its theoretical basis is rather firmly established. A summary with pertinent diagrammatic charts has recently been published by Clark (5).

A great deal remains to be done, not only in providing indicators more closely or more evenly graded with respect to their characteristic potentials, but also indicators which, having the potentials required for particular purposes, also have other properties suited to those purposes.

REFERENCES

- (1) BILLMANN, E.: *Ann. chim.* **9**, 109 (1921).
- (2) The Works of Robert Boyle, Vol. II, p. 47. London (1744).
- (3) *Ibid*, p. 53, Experiment XX.
- (4) CLARK: *J. Wash. Acad. Sci.* **10**, 255 (1920).
- (5) CLARK: *Medicine* **13**, 207 (1934).
- (6) CONANT, KAHN, FIESER, AND KURTZ: *J. Am. Chem. Soc.* **44**, 1382 (1922).
- (7) *Encyclopedie Methodique, Chimie et Metallurgie*, Vol. IV, p. 66.
- (8) FARADAY, MICHAEL: *Chemical Manipulations*, 1st American edition, pp. 284-6. Philadelphia (1831).
- (9) GILLESPIE: *Soil Sci.* **9**, 199 (1920).
- (10) GRANGER, F. S., AND NELSON, J. M.: *J. Am. Chem. Soc.* **43**, 1401 (1921).
- (11) HOFFMAN, FREDERIC: *Dissertation physico-medic. select.*, p. 183. Leyden (1708).
- (12) PASTEUR, L.: *Compt. rend.* **87**, 33 (1878).
- (13) SØRENSEN, S. L. P.: *Biochem. Z.* **21**, 131, 201 (1909).
- (14) VON HELMHOLTZ, H.: *Arch. Anat. Physiol. Med.*, p. 453 (1843).

THE COLORIMETRIC DETERMINATION OF HYDROGEN-ION CONCENTRATION IN AQUEOUS SOLUTION

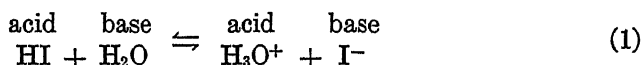
MARTIN KILPATRICK

Department of Chemistry, The University of Pennsylvania, Philadelphia, Pennsylvania

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The literature abounds with papers on the subject of the determination of pH, but even to-day there is a great deal of confusion as to the relative merits of the various methods available. A part of this confusion arises from the definition of the term pH, and another part arises from misunderstanding and neglect of salt effects (6). In many cases the worker talks and thinks in terms of concentration of hydrogen ion, but measures something approaching the activity of the hydrogen ion. In the use of the colorimetric method great care is often taken in making the measurements and all too little thought given to the calculation of the result. In order to avoid confusion, in the present paper results will be expressed not in terms of pH, but in actual hydrogen-ion concentrations in moles per liter.

The substances used for the colorimetric determination of hydrogen-ion concentration are acids and bases, of which the acid form or basic form (or both) is colored. In the case of a weak monobasic acid, HI, the double acid-base equilibrium with the solvent can be represented in the following manner



By increasing the concentration of the base I^- , the solution can be buffered in respect to the hydrogen ion H_3O^+ . If HI or I^- is colored, we have an indicator. The fact that the indicator establishes its own buffer equilibrium is of great importance in the determination of the hydrogen-ion concentration of unbuffered or poorly buffered solutions. For example, if we are determining the hydrogen-ion concentration of carbon dioxide-free water, with a hydrogen-ion concentration of $1 \times 10^{-7}M$, and we add an indicator, the hydrogen-ion concentration is no longer $1 \times 10^{-7}M$. This problem will be discussed in a later section of the paper. In the case of well-buffered solutions this problem does not arise, for here the constituents of the buffer system of the indicator are present at concentrations of

the order of $10^{-5}M$, while the constituents of the buffer system whose hydrogen-ion concentration we are measuring are usually present at concentrations of the order of 10^{-1} or $10^{-2}M$.

The equilibrium involved in equation 1 can be formulated by the mass law as follows

$$K_c = c_{H_3O^+}c_{I^-}/c_{HI} \quad (2)$$

where K_c represents the classical dissociation constant. When the concentration of HI is equal to that of I^- , that is, when the indicator is half transformed, we have

$$K_c = c_{H_3O^+} \quad (3)$$

Now K_c varies with electrolyte concentration so that the half-change point in one solution may not be the half-change point in another, even though the hydrogen-ion concentrations are the same. This means that equal color for equal indicator concentration does not always show equal hydrogen-ion concentration, and I might add that it does not always show equal hydrogen-ion activity. The fundamental equation for two solutions of equal indicator concentration and equal color is

$$(c_{H_3O^+}/K_c)_I = (c_{H_3O^+}/K_c)_{II} \quad (4)$$

Letting solution I be the known, there results for the hydrogen-ion concentration of the unknown solution

$$(c_{H_3O^+})_{II} = (c_{H_3O^+})_I(K_c)_{II}/(K_c)_I \quad (5)$$

If the ratio $(K_c)_{II}/(K_c)_I$ is known as well as $(c_{H_3O^+})_I$, $(c_{H_3O^+})_{II}$ can be calculated.¹

I. THE DETERMINATION OF HYDROGEN-ION CONCENTRATION BY COMPARISON WITH BUFFER STANDARDS

The standards for the determination of hydrogen-ion concentration are most conveniently prepared from monobasic acids and their salts, and potassium chloride. If the classical dissociation constant of the acid is known at the electrolyte concentration chosen, the standards can be made up from standard solutions of the weak acid and carbonate-free sodium hydroxide, and the neutral salt. For example, the classical dissociation constant of acetic acid in 0.1 *M* potassium chloride solution has been determined kinetically and electrometrically (9) and the values found are 2.90 and 2.84×10^{-5} , respectively. Both methods involve assumptions, but

¹ For the corresponding equations in terms of activity of hydrogen ion, see references 6 and 7.

the fact that the results agree within 3 per cent indicates the validity of the assumptions. If we take K_c for acetic acid as 2.90×10^{-5} , and prepare a solution 0.0100 M in sodium acetate, 0.0100 M in acetic acid, and 0.09 M in potassium chloride, we know its hydrogen-ion concentration within 3 per cent (0.01 pH unit) from equation 2. By varying the concentration of acetic acid from 0.05 to 0.002 M , a series of safely buffered standards can be prepared covering the range of hydrogen-ion concentration from (5) (2.90×10^{-5}) to (0.2) (2.90×10^{-5}) M .

There is given in table 1 the information necessary for the preparation of standard buffer solutions covering the range from 1×10^{-2} to 2×10^{-7} M in hydrogen-ion concentration. The second column of the table contains the thermodynamic dissociation constant, given for purposes of comparison; the third, the classical dissociation constant in 0.1 M potassium

TABLE 1

The classical dissociation constants of certain acids in 0.1 M potassium chloride solution at 25°C.*

ACID	$K_a(c = 0)$	$K_a(c = 0.1)$	INDICATOR	$K_a(c = 0.1)$
Monochloroacetic...	1.396×10^{-3}	2.42×10^{-3}	Thymol blue pink-yellow	2.04×10^{-2}
Formic ..	1.86×10^{-4}	3.00×10^{-4}	Methyl orange	4.27×10^{-4}
Glycolic.. . . .	1.46×10^{-4}	2.38×10^{-4}		
Benzoic	6.312×10^{-5}	10.12×10^{-5}	Bromophenol blue	14.9×10^{-5}
			Bromocresol green	3.07×10^{-5}
Acetic...	1.745×10^{-5}	2.90×10^{-5}	Methyl red	1.04×10^{-5}
			Chlorophenol red	1.10×10^{-6}
Cacodylic	6.0×10^{-7}	8.49×10^{-7}	Bromocresol purple	9.3×10^{-7}

* The total concentration of uni-univalent electrolyte, $c_{KCl} + c_{NaX}$ is 0.1 M . $c_{NaX} < c_{KCl}/5$.

chloride solution, as determined electrometrically or kinetically in this laboratory. In the fourth column are listed indicators suitable for use with the acid in question, and in the fifth is given the value of the classical dissociation constant of the indicator in 0.1 M potassium chloride solution.

Hydrogen-ion concentrations higher than 5×10^{-3} can be obtained by the use of hydrochloric acid or perchloric acid. For concentrations lower than 2×10^{-7} M , other buffer systems are available; for these data are to be found in the literature. Standards can be prepared at intervals of 5 per cent change in hydrogen-ion concentration. It is suggested that new standards be made up frequently from standard acid and base, since the indicator colors fade and the buffer solutions often decompose on standing.

Table 2 gives the $K_c/K_{c, 0.1}$ ratios for a number of indicators at various ionic strengths. The solvent salt is potassium chloride.

To determine the hydrogen-ion concentration of an unknown, the un-

known, containing indicator at the same concentration as the standards, is matched against the standards after the procedure of Clark (3). The hydrogen-ion concentration of the matching standard is then multiplied by the factor in table 2 corresponding to the ionic strength of the unknown.

TABLE 2
K_c/K_{c,0.1} ratios in potassium chloride solution at 25°C.

MOLES SALT PER LITER	THYMOL BLUE	BROMOPHE- NOL BLUE	CHLORO- PHENOL RED	BROMOCRE- SOL GREEN	BROMO- CRESOL PURPLE	METHYL RED	METHYL ORANGE
0.1	1.00	1.00	1.00	1.00	1.00	1.00	1.00
0.2		1.17					1.02
0.5	1.03	1.29	1.22	1.31	1.25	0.89	0.67
1.0		1.25	1.48	1.18	1.32	0.75	0.61
1.5		1.15	1.20	1.13	1.02	0.60	
2.0		1.06	1.20	0.95	0.91	0.51	0.33
2.5		0.95	0.86	0.83	0.82	0.35	
3.0		0.76	0.72	0.77	0.67	0.28	0.16

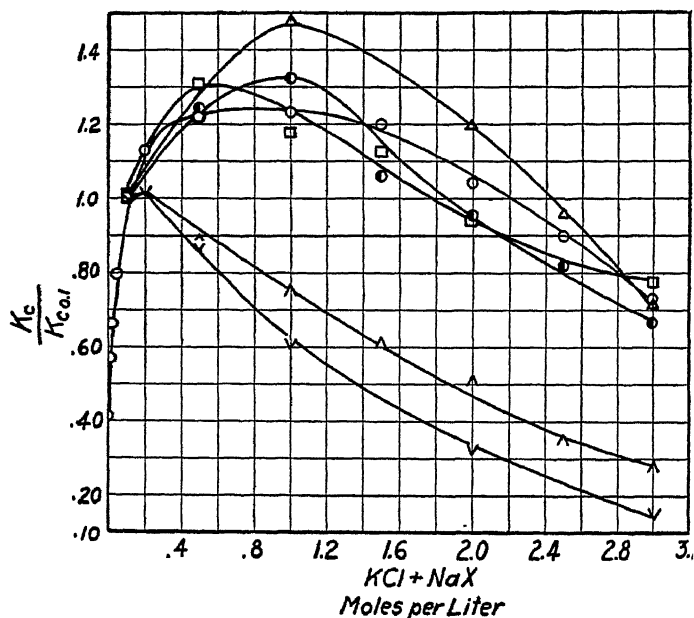


FIG. 1

For ionic strengths between 0.01 and 0.1, the values for bromophenol blue from table 3 can be used for the other sulfonphthaleins. For intermediate points the factor can be read from a plot similar to that shown in figure 1. The results are expressed in moles of hydrogen ion per liter and should be accurate to 5 per cent (0.02 pH unit).

Strictly speaking, the electrolyte in the unknown should be potassium chloride. At low ionic strengths (below 0.1) the error arising from the use of a different solvent salt is quite negligible. To show its magnitude at higher concentrations, in table 4 are given the values of the ratio $K_c/K_{c(0.1 \text{ KCl})}$ for the indicator bromophenol blue in solutions of four other uni-univalent salts, as well as in solutions of potassium chloride.

As pointed out elsewhere, no general method of expressing these second-order salt effects has as yet been found. Each salt has a specific effect on the dissociation constant of the indicator, and this becomes evident even

TABLE 3
 $K_c/K_{c(0.1 \text{ KCl})}$ ratios for bromophenol blue in dilute solution

MOLES ELECTROLYTE PER LITER	$K_c/K_{c(0.1 \text{ KCl})}$	MOLES ELECTROLYTE PER LITER	$K_c/K_{c(0.1 \text{ KCl})}$
0	0.41	0.01	0.57
0.0015	0.47	0.025	0.66
0.003	0.48	0.05	0.79
0.006	0.54	0.10	1.00

TABLE 4
 $K_c/K_{c(0.1 \text{ KCl})}$ ratios for bromophenol blue

MOLES SALT PER LITER	KCl	NaCl	LiCl	NaClO ₄	$p\text{-C}_6\text{H}_4\text{CH}_2\text{SO}_3\text{-Na}$
0.1	1.00	1.05	1.07	1.01	1.01
0.2	1.17	1.19	1.24	1.07	1.04
0.4	1.31	1.22	1.34	1.07	0.99
0.6	1.31	1.25	1.37	1.04	0.89
0.8	1.30	1.27	1.33	1.00	0.74
1.0	1.25	1.26	1.32	0.91	0.64
1.5	1.15	1.10	1.13	0.76	
2.0	1.06	0.93	0.91	0.62	
2.5	0.95				
3.0	0.76	0.56	0.50	0.36	

at low concentrations when one is able to determine the differences accurately. The advantages of the method presented here are that it relates the salt error directly to the basic equation, that it makes the error immediately apparent, and that it offers a simple correction.

II. DETERMINATION OF HYDROGEN-ION CONCENTRATION WITHOUT BUFFER STANDARDS

It is possible to determine hydrogen-ion concentrations colorimetrically without the use of buffer solution standards. The method employed is the well-known Gillespie method (5) in which the reference solutions are

two solutions containing the indicator in its complete acid and basic form, respectively. A compensating colorimeter similar to that described by Clark (3) enables rapid determination of the ratio of acid to basic form of indicator in the unknown solution. It is important that the concentration of indicator be the same in the two standards and in the unknown. A microburet is a convenience in adding the indicator. At this point it seems desirable to mention that care must be taken in regard to the stability of the color, particularly the color of the basic form.

TABLE 5

Progressive change in colorimeter readings for alkaline solutions of bromophenol blue
Temperature, $25^{\circ} \pm 3^{\circ}\text{C}$. Bromophenol blue concentration, $2 \times 10^{-5} \text{ M}$. Reference standard, freshly prepared basic form; reading, 20.0

DAYS	MOLES PER LITER								
	0.001* NaOH	0.001† NaOH 0.10 KCl	0.002 NaOH	0.003 NaOH	0.003 NaOH 0.10 KCl	0.005 NaOH	0.008 NaOH	0.009 NaOH	0.009 NaOH 0.10 KCl
1	19.6	19.2	18.6		16.9	16.6	14.6		11.3
2	19.0	18.1	17.6	16.8	14.1	14.0	10.6	11.1	8.4
3	18.4	16.9	16.7	15.4		11.4	7.8	7.9	
4	18.1	16.2		14.5	9.6			6.1	1.9
5	17.6	14.9	15.0	13.2		8.3	4.3	5.0	
6	16.8	14.0		11.9	6.4			3.3	0.9
7	16.2	13.1	13.0	10.7	5.0	5.5	2.3	2.4	0.6
8	15.8	12.0	12.0		4.3	4.4	1.8		
9	15.7	11.1	11.1	8.8	3.4	3.5	1.3	1.5	
10	15.1		10.4			3.1	1.1		Colorless
11	14.8			6.9				0.9	
12	14.4	9.0		6.2				0.6	
13	13.8	8.3		5.6	1.9		Colorless	Colorless	
14	12.7			5.0		1.8			
15			8.2						
16					Colorless				
18	11.9			3.5					

Solutions marked * represent the average of six experiments; those marked †, the average of three.

To show how rapidly the color of the standard may change, there are recorded in table 5 the results of a series of experiments on bromophenol blue in sodium hydroxide solution. These experiments were carried out with C. E. Gulezian in 1930. The data are presented graphically in figure 2.

The experiments were not carried out in a thermostat; nevertheless it is apparent from table 6 that the time required for the color to fade to one

half its original intensity is proportional to the concentration of sodium hydroxide. When potassium chloride is present the fading is much more rapid. From Gulezian's experiments it is evident that only enough alkali for conversion of the indicator to the basic form should be used.

A possible explanation of the fading has been given elsewhere (2). Calculation of the time of half-change, for lower hydroxyl-ion concentrations, indicates that a reaction with rate proportional to the hydroxyl-ion con-

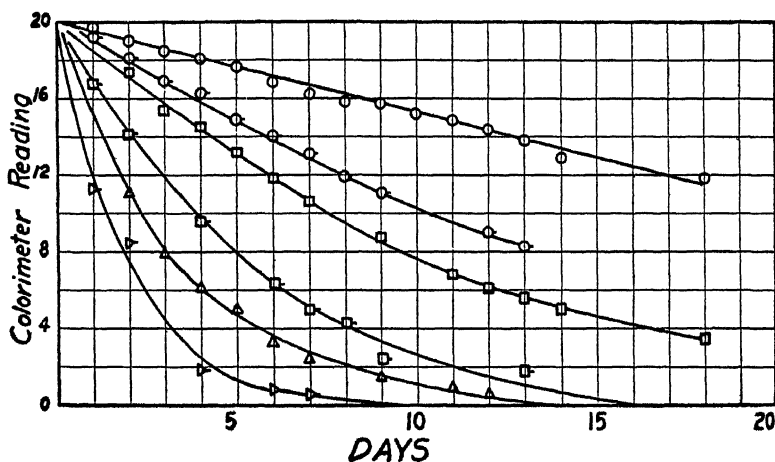


FIG. 2

TABLE 6

Fading of bromophenol blue in alkaline solution

MOLES NaOH PER LITER	APPROXIMATE TIME OF HALF-CHANGE
	<i>days</i>
0.001	20-22
0.002	10-11
0.003	7.5
0.005	4
0.009	2.3

centration is not the only one taking place. For we have observed, as have others (11), a fading of the color in solutions of much lower hydroxyl-ion concentration. The fading is not restricted to the halogen-containing sulfonphthaleins.

Having determined the acid-base ratio, one can calculate the hydrogen-ion concentration of the unknown from equation 2. As already pointed out, the classical dissociation constant of the indicator varies with the

nature and concentration of the electrolyte present, so that the proper value of K_c must be known. Table 7 gives the classical dissociation constants of a number of indicators in potassium chloride solutions of various ionic strengths. The values marked G were obtained by Güntelberg and Schiödt (6) at 18°C.; those marked K are computed from values compiled by Kolthoff (12), and the others are from this laboratory.

The dissociation constants of the indicators are most conveniently determined by the Gillespie method. The procedure is that just described, the only difference being that the hydrogen-ion concentration of the solution

TABLE 7

Classical dissociation constants in potassium chloride solution at $25^\circ \pm 3^\circ\text{C}$.

MOLES ELECTRO- LYTE PER LITER	THYMOL BLUE $\times 10^2$	BROMO- PHENOL BLUE $\times 10^6$	CHLORO- PHENOL RED $\times 10^7$	BROMOCRE- SOL GREEN $\times 10^6$	BROMOCRE- SOL PURPLE $\times 10^7$	METHYL RED $\times 10^6$	METHYL ORANGE $\times 10^4$
0	2.04 (K)	6.0	5.4	1.15 (K)	3 0 3.8 (K)	10 0 (K)	3 23 (G)
0.01		8 5	7.4	1 56 (K)	5.5 (K)		
0.025		9.9					
0.05	2 29 (K)	11.7	9 8	2.07 (K)	6.8 (K)		
0.1	2.32 (K)	14 9	11 0	3 07 2 33 (K)	9 3	10.4	4 27 (G)
0.2		17.4					4.34 (G)
0.3		17.9			11.2		
0.4		19 6					
0.5	2.38 (K)	19.2	13 4	4.03	11 6	9.21	3.71 (G)
0.6		19.5					
0.7		19.7			12.6		
0.9		19.3					
1.0		18.7	16.2	3.61	12.3	7.75	2.62 (G)
1.5		17.1	13.1	3.46	11.0	6.25	
2.0		15.8	13.2	2.93	8.9	5 33	1.40 (G)
2.5		14.1	9 45	2.55	7.6	3.61	
3.0		11.3	7.90	2 38	6 2	2.90	0.69 (G)

examined is known from previous electrometric or kinetic (8, 9) or even colorimetric (7, 9) measurements. In all cases the primary standard is a solution of a strong acid.

III. DETERMINATION OF THE HYDROGEN-ION CONCENTRATION IN UNBUFFERED SOLUTIONS OF LOW HYDROGEN-ION CONCENTRATION

In measuring the hydrogen-ion concentration of an unbuffered or weakly buffered solution it is necessary first of all to determine whether or not the addition of the indicator has changed the hydrogen-ion concentration. To

do this one must carry out a series of measurements at several indicator concentrations and several acid-base ratios of the indicator (1, 4, 11, 13). In principle the method of determining the hydrogen-ion concentration of the unknown consists in finding an indicator solution of such an acid-base ratio that its addition does not alter the hydrogen-ion concentration. Comparison can then be made with the standard buffer solutions and the correction for the salt error made from table 2 or 3, or, if complete acid and basic standards are employed, from table 7.

For unbuffered or very weakly buffered solutions Acree and Fawcett (1, 4) recommend the use of a series of standard solutions of the indicator, adjusted in steps of 0.2 pH unit (70 per cent in hydrogen-ion concentration). By matching against buffer standards, they determine which of their adjusted indicator solutions does not change color upon addition of the unknown, and call this indicator solution "isohydric" with the unknown. The pH as read off is corrected for salt error if necessary. Kolthoff and Kameda (13) state that it is not worth while to prepare a series of adjusted indicator solutions, since these solutions are not stable. They advocate approaching the correct acid-base ratio of indicator empirically. When the correct adjustment is found, comparison with buffer standards shows the same pH for different concentrations of indicator. Both Acree and Fawcett, and Kolthoff and Kameda, emphasize the necessity of using pure, carbon dioxide-free water, and of preventing the entrance of carbon dioxide during the test. To be consistent, it should be said that these investigators define the salt error as the difference between the colorimetric and electrometric pH values, and that the pH values as given by them are not equal to the negative logarithm of the hydrogen-ion concentration (10). For experimental details, and for references to other work on unbuffered solutions reported in the literature, the reader is referred to the papers of Acree and Fawcett and of Kolthoff and Kameda.

SUMMARY

1. The fundamental equation for the determination of hydrogen-ion concentration by the colorimetric method has been discussed.
2. A set of *hydrogen-ion concentration* standards is suggested, and the data necessary for the preparation of the standards furnished.
3. Indicators suitable for use with the standards have been listed, and their dissociation constants given.
4. A simple and direct method of correcting for salt error is presented, together with the data necessary for making the correction when measurements are made in the presence of certain of the more common uni-univalent solvent salts.

REFERENCES

- (1) ACREE, S. F., AND FAWCETT, E. H.: *Ind. Eng. Chem., Anal. Ed.* **2**, 78 (1930).
- (2) CHASE, E. F., AND KILPATRICK, M.: *J. Am. Chem. Soc.* **54**, 2284 (1932).
- (3) CLARK, W. M.: *The Determination of Hydrogen Ions*, 3rd edition. The Williams & Wilkins Co., Baltimore (1932).
- (4) FAWCETT, E. H., AND ACREE, S. F.: *J. Bact.* **17**, 163 (1929).
- (5) GILLESPIE, L. J.: *J. Am. Chem. Soc.* **42**, 742 (1920).
- (6) GÜNTELBURG, E., AND SCHIÖDT, E.: *Z. physik. Chem.* **135**, 393 (1928).
- (7) KILPATRICK, M.: *J. Chem. Education* **9**, 1017 (1932).
- (8) KILPATRICK, M., AND CHASE, E. F.: *J. Am. Chem. Soc.* **53**, 1732 (1931).
- (9) KILPATRICK, M., CHASE, E. F., AND RIESCH, L. C.: *J. Am. Chem. Soc.* **56**, 2051 (1934).
- (10) KILPATRICK, M., AND KILPATRICK, M. L.: *J. Chem. Education* **9**, 1010 (1932).
- (11) KOLTHOFF, I. M.: *Biochem. Z.* **168**, 110 (1926).
- (12) KOLTHOFF, I. M.: *J. Phys. Chem.* **34**, 1466 (1930).
- (13) KOLTHOFF, I. M., AND KAMEDA, T.: *J. Am. Chem. Soc.* **53**, 825 (1930).

REACTION RATES AND INDICATOR ACIDITIES

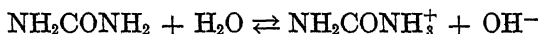
LOUIS P. HAMMETT

Department of Chemistry, Columbia University, New York City

Received December 10, 1934

Since the general adoption of the Arrhenius theory the usual quantitative measure of acidity has been hydrogen-ion concentration or sometimes hydrogen-ion activity. It is a measure which is based entirely upon the behavior of dilute aqueous solutions. So long as chemists generally were content to restrict their theoretical investigations to these solutions it was a moderately successful one, but it leads to inextricable confusion when it is extended to non-aqueous solutions or to concentrated aqueous ones. There is therefore an almost irresistible tendency to set up a measure of acidity which shall be capable of this extension without confusion or ambiguity, and some difference of opinion about the procedure to be adopted (4). The criterion of acidity in terms of a measurement with a basic indicator, which was suggested by Hammett and Deyrup (18), is unambiguous, historically reasonable, and measurable. But the real justification for its adoption, as for the adoption of any definition, must lie in its utility. It is therefore extremely important that this criterion of acidity makes it possible to predict from an indicator measurement the rate at which sucrose is hydrolyzed in 4 molar hydrochloric acid or the rate of the Beckmann rearrangement of acetophenone oxime in 95 per cent sulfuric acid, and that this correlation promises to lead to a clearer insight into the nature and mechanism of these and similar reactions.

The problem of a measure of acidity is most easily stated in terms of an extremely weak base such as urea. In water this reacts to a minute extent according to the reaction



the equilibrium constant being not far from 10^{-14} . If formic or sulfuric acid is added, more of the base NH_2CONH_2 is converted to the cation $\text{NH}_2\text{CONH}_3^+$. This process of converting a base B to the corresponding cation BH^+ is so important as to deserve a name of its own, and it will be referred to in this article as the salt formation or the ionization of the base. In particular the ratio of the concentrations of cation and base $C_{\text{BH}^+}/C_{\text{B}}$ will be called the ionization ratio of the base. In sufficiently dilute solu-

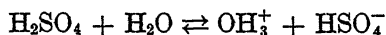
tions there is direct proportionality between the ionization ratio and the hydrogen-ion concentration, the equation

$$C_{H^+} = K \frac{C_{BH^+}}{C_B} \quad (1)$$

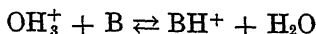
being a simple and direct consequence of the mass law.

As the concentration of the acid increases, however, deviations from this simple law appear and rapidly increase in magnitude. Eventually a point is reached beyond which the conductivity of a sulfuric acid-water mixture decreases, but the tendency toward salt formation with a weak base does not. Consequently pure formic or sulfuric acids are very slightly ionized, but they are nevertheless capable of converting such weak bases as urea practically completely to the cation (19, 20). Now it has seemed to many people, following the lead of Hantzsch (23), that the extent of salt formation or ionization of a weak base is so closely related to the original and fundamental concepts of acidity upon which the ionization theory grafted the idea of hydrogen-ion concentration that the salt formation criterion should be accepted when the two disagree. On this basis pure formic or sulfuric acids are said to be more acidic than the highly ionized dilute aqueous solutions because the pure acids react more completely with weak bases.

The explanation of the divergent behavior of conductivity and salt formation in the sulfuric acid-water solutions is to be found in a hypothesis, also due to Hantzsch (23), according to which sulfuric acid does not dissociate into ions when it is dissolved in water, but rather reacts with the base, water,



to form an oxonium ion, OH_3^+ , which bears the same relation to water that ammonium ion does to ammonia. There is indeed strong evidence from a variety of sources that the substance conventionally referred to as hydrogen ion in dilute aqueous solutions is really oxonium ion. This has been reviewed elsewhere (16). The conductivity due to a reaction of this sort must obviously reach a maximum somewhere in the neighborhood of an equimolar mixture of acid and water. On the other hand, the very fact that the reaction occurs demonstrates that hydrogen ions are less firmly bound, are more available for reaction with weak bases, in H_2SO_4 than they are in OH_3^+ . The first effect of increasing the proportion of H_2SO_4 in a sulfuric acid-water mixture is to increase the concentration of OH_3^+ . By mass action this increases the tendency toward salt formation of weak bases by the reaction



With further increase in the proportion of acid, a point is reached beyond which the concentration of OH_3^+ decreases rather than increases, but it decreases only by virtue of an increase in the concentration of free, unreacted H_2SO_4 . Since the H_2SO_4 carries less firmly bound hydrogen ion, it has, mole for mole, a greater tendency for salt formation with weak bases than does OH_3^+ . The ionization ratio of a weak base continues therefore to increase with increasing acid concentration, although the concentration of OH_3^+ decreases.

To give these qualitative ideas a quantitative meaning some method of determining the extent of ionization of weak bases is required, and the simplest and most obvious method is to use bases which have the properties of an indicator. For a simple basic indicator is merely a monoacid base whose ionization or salt formation process is accompanied by a change in light absorption in the visible region. From this change the ionization ratio can be determined by the methods of colorimetry. If a given indicator is measurably ionized in two solutions,¹ the relative extent of that ionization in the two solutions is a measure of their relative acidities in terms of the salt formation criterion. The range of acidity accessible to investigation by any one indicator is of course limited; at too low acidities the concentration of the ion BH^+ cannot be detected or measured, at too high acidities the same thing is true of the base B. If, however, the ranges of two indicators overlap, the relative strengths of the two indicator bases can be determined by determining their degrees of ionization in some solution whose acidity lies within the overlapping portion of the ranges. With this knowledge it becomes possible to compare by indicator measurements the relative acidities of two solutions, one of which is measurable only by the first indicator, the other only by the second. If the second indicator range overlaps the range of a third, the relative strengths of the first and third indicators may be obtained even though they cannot be directly compared. A still further range of acidities is thereby opened to investigation, and a fourth and more indicators may of course be added in the same way.

In mathematical language these ideas take the following form: the criterion of the strength of a base B is the quantity (18)

$$\text{p}K' = -\log \frac{a_{\text{H}^+}a_{\text{B}}}{a_{\text{BH}^+}} \quad (2)$$

where the a 's are activities. (This is really the logarithmic acidity constant of the acid BH^+ (3).) The measure of acidity is the acidity function H_0

¹ It is of course necessary that the amount of indicator be so small that its addition does not appreciably change the acidity of the solution.

defined by the equation (18)

$$H_0 = pK' - \log C_{BH^+}/C_B \quad (3)$$

It is determined experimentally by the colorimetric measurement of the ionization ratio C_{BH^+}/C_B , the value of pK'_B being determined by comparison with other indicator bases. The whole series of indicators is standardized in such a way that the acidity function H_0 becomes equal to the ordinary pH in dilute aqueous solutions.

It should be emphasized that the value of H_0 is exactly the measure of acidity that would be obtained if one forgot all about hydrogen-ion activities, about activity coefficients, and about the salt error of indicators, and set about in the simplest way possible to determine the pH of a solution by using basic indicators.² It would be quite justified therefore to call the H_0 value the "pH by a basic indicator." It must be realized, however, that it would not in general be equal to the electrometric pH even within the limited range in which an electrometric pH measurement has any meaning. It would also differ from the quantity which might be called the "pH by an acid indicator," for which the symbol H_- has been proposed (18), but it must certainly be a better measure of the behavior of the solution toward weak uncharged bases than either electrometric pH or H_- .

The justification for this apparently naive procedure is best given in terms of another expression for H_0 which may easily be shown to be equivalent to equation 3:

$$H_0 = - \log a_{H^+} f_B / f_{BH^+} \quad (4)$$

Here a_{H^+} is the activity of hydrogen ion, and the f 's are the activity coefficients of the base B and the cation BH^+ . It is clear from this equation that the value of H_0 will be independent of the particular base used for the measurement only if the ratio f_B/f_{BH^+} has the same value for all bases in any given medium. Unfortunately this is not exactly true (5, 15, 17); it is perhaps not even approximately true in extreme cases. It has, however, been possible to show that the requirement is fulfilled to a satisfactory precision for mixtures of the four strong acids, sulfuric, perchloric, hydrochloric, and nitric, with water, and for anhydrous formic acid (18, 21). Within this range of media, which turns out to be an interesting and practically important one, the value of H_0 has a general meaning and usefulness which is independent of the particular base used for the measurement.

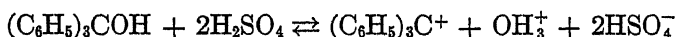
² Of course the simplicity must not extend to a neglect of the chemical and electrical nature of the indicators. They must be simple basic indicators in the sense that their color change is actually a measure of the extent of conversion of a neutral base B to an ion BH^+ . There are ways of making certain of this (see reference 18, p. 2723).

Table 1 lists the indicators which have been studied in this way, together with the pK' constants obtained in various media (18, 21). It will be noted that only the first two are commonly recognized as indicators, and that even these are not among the most familiar ones; further that four of them depend for their basic properties upon an oxygen atom instead of upon a nitrogen atom. The unfamiliarity depends partly of course upon the fact that these indicators are designed for the investigation of a higher range of acidities than is the case with those used in dilute aqueous solutions, but even more upon the requirement that they be simple monoacid bases. The indicators used in aqueous solutions are in fact poorly suited

TABLE 1
Basic strength of indicators (18, 21)

INDICATOR	HCl- H ₂ O	HNO ₃ - H ₂ O	H ₂ SO ₄ - H ₂ O	HClO ₄ - H ₂ O	HCOOH
Aminoazobenzene.....	+2.80				
Benzeneazodiphenylamine.....	+1.52				
<i>p</i> -Nitroaniline.....	+1.11	[+1.11]	[+1.11]	[+1.11]	
<i>o</i> -Nitroaniline ...	-0.17	-0.20	-0.13	-0.19	[-0.17]
<i>p</i> -Chloro- <i>o</i> -nitroaniline... ..	-0.91	-0.97	-0.85	-0.91	-0.94
<i>p</i> -Nitrodiphenylamine... ..			-2.38		-2.51
2,4-Dichloro-6-nitroaniline.. ..			-3.22	-3.18	-3.31
<i>p</i> -Nitroazobenzene.....			-3.35	-3.35	-3.29
2,6-Dinitro-4-methylaniline.....			-4.32		
2,4-Dinitroaniline... ..			-4.38	-4.43	
<i>N,N</i> -Dimethyl-2,4,6-trinitroaniline.			-4.69		
Benzalacetophenone.....			-5.61		
β -Benzoylnaphthalene.....			-5.92		
<i>p</i> -Benzoyldiphenyl.....			-6.19		
6-Bromo-2,4-dinitroaniline.....			-6.59		
Anthraquinone.....			-8.15		
2,4,6-Trinitroaniline.....			-9.29		

to the investigation of changing media. They commonly contain sulfonic acid groups which increase their water-solubility, but greatly complicate the interpretation of salt and medium effects. Their brilliance of color is frequently associated with a triphenylcarbinol structure, and triphenylcarbinol is known to react with acids according to equations such as



The formation of water in the ionization makes the ionization ratio specifically dependent upon the activity of water, and therefore no unique measure of acidity. There is finally some indication that they have been selected to give as close an approximation over as wide a range as possible

to the electrometric pH, and this can only result from very specialized and complex compensations of opposing effects (2).

The range of base strength covered by this list of indicators is very wide, the strongest base involved, aminoazobenzene, which has an indicator range about the same as that of methyl orange, is 10^{12} stronger than the weakest one, trinitroaniline, which is not completely ionized in pure sulfuric acid.

It may be easily shown that a failure of the fundamental requirement that the ratio f_B/f_{BH^+} be the same for all bases in a given medium would lead necessarily to differences in the pK' values obtained for a single base in different media. The agreement between the values for these five media, which is probably as good as the colorimetric method permits, demonstrates therefore the satisfaction of the requirement in this range.

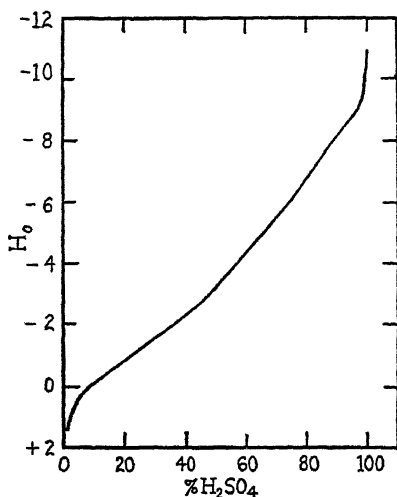


FIG. 1. Acidity function of $H_2SO_4 - H_2O$ solutions

Figure 1 shows the variation of H_0 with percentage composition of sulfuric acid-water mixtures (18, 21). It clearly exhibits the continuous increase in acidity with increasing acid concentration, which was previously mentioned. The very great acidity of pure sulfuric acid is shown by the large negative value of H_0 , nearly -11 , obtained. It seems probable that fuming sulfuric acid is even more acidic than this.

Figure 2 shows the variation of H_0 with molality for five acids in moderately concentrated aqueous solution (21). The behavior of the transition acid, trichloroacetic acid, differs strongly from that of the four strong ones.

The crucial test of this whole system is to be found in its usefulness and especially in its ability to predict reaction rates and to assist in the inter-

pretation of reaction mechanisms. The problem of reaction rates in highly acid solutions may be approached in very much the same simple fashion that was used in setting up the scale of acidity. In a dilute aqueous solution the rate of an acid-catalyzed reaction is frequently, although as Brönsted has shown (6), not always, proportional to the concentration of hydrogen ion. The velocity constant k_v is then given by $k_v = k_0 c_{H^+}$, where k_0 is a proportionality constant. This may be put in a form very suitable for a test of its applicability by taking logarithms

$$\log k_v = -\text{pH} + \log k_0$$

If the equation holds, a plot of $\log k_v$ against pH is a straight line whose slope is -1 .

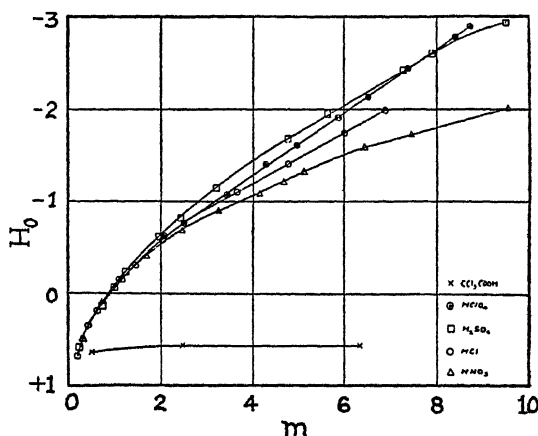


FIG. 2. Acidity functions of moderately concentrated aqueous acids

Since the acid catalysis may be supposed to depend upon the addition of hydrogen ion to a very weak base, sucrose, ethyl acetate, or the like, that is, upon a process which is very similar to the ionization of a simple basic indicator, it seems natural to look for a similar correlation between k_v and H_0 in more concentrated acid solutions. Figure 3 shows such a test for that veritable classic of reaction velocity experiments, the sucrose hydrolysis (22). There is perfect agreement for the four strong acids at concentrations extending far beyond the region of dilute solutions. Within that region it has of course been long recognized and amply demonstrated that the reaction rate is proportional to the concentration of hydrogen ion; but all kinds of attempts to correlate the rate with some sophisticated measure of acidity in more concentrated acid solutions have failed. By contrast there is here demonstrated a direct proportionality between reac-

tion rate and the measure of hydrogen-ion concentration or activity obtained by an almost naive use of basic indicators without consideration of salt or medium effects.

Figure 4 shows a similar successful correlation for the hydrochloric acid-catalyzed hydrolysis of ethyl acetate and for the nitric acid-catalyzed hydrolysis of cyanamide (22).

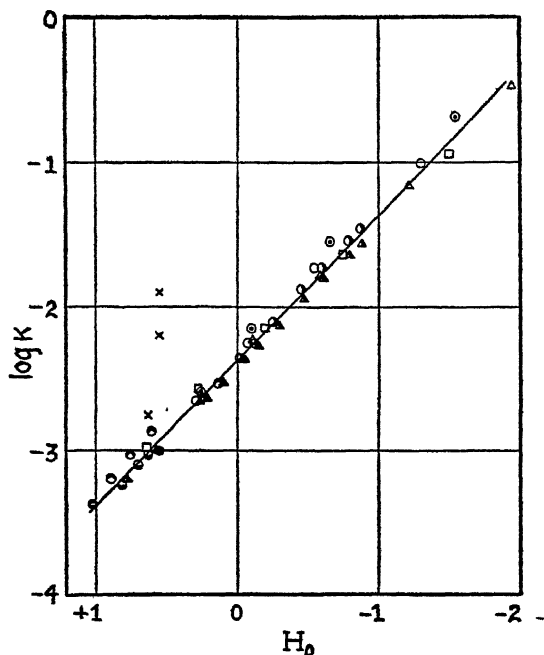


FIG. 3. Relation between H_0 and velocity constant for hydrolysis of sucrose. $\odot$, 0.5–4 M $HClO_4$; $\square$, 0.25–3.77 M H_2SO_4 ; $\circ$, 0.5–4 M HCl ; $\triangle$, 0.5–6.95 M HNO_3 ; $\times$, 0.5–4 M CCl_3COOH , all from data of Hantzsch and Weissberger. $\bullet$, 0.28–3.08 M HCl ; $\blacktriangle$, 0.19–3.08 M HNO_3 , data of Armstrong and Wheeler and of Worley. $\ominus$, 0.1 N HCl + 0–3 M KCl ; $\ominus$, 0.1 N HCl + 0–1.3 M $BaCl_2$, data of Kautz and Robinson.

There are, however, acid-catalyzed reactions, for instance the hydrolysis of hydrocyanic acid or the rearrangement of acetylchloroaminobenzene, which exhibit no parallelism whatsoever between reaction rate and indicator acidity. And even in the sucrose case the rate of the hydrolysis by the transition acid, trichloroacetic, deviates widely from the theoretical line with which the values for the strong acids agree so closely. Whatever the reason for these differences, and much more experimental information will be necessary if any assurance on this question is to be obtained, they represent very definitely a classification of reactions occurring in concentrated

acid solutions into those that do and those that do not exhibit a parallelism between reaction rate and acidity function. The difference must depend upon some fundamental contrast in mechanism, and its recognition cannot but assist in the further interpretation and understanding of the catalytic process.

The sucrose and ester hydrolyses are typical cases of acid catalysis. But the same relation between reaction rate and acidity function holds for some reactions of an apparently quite different sort which take place at much higher acid concentrations.

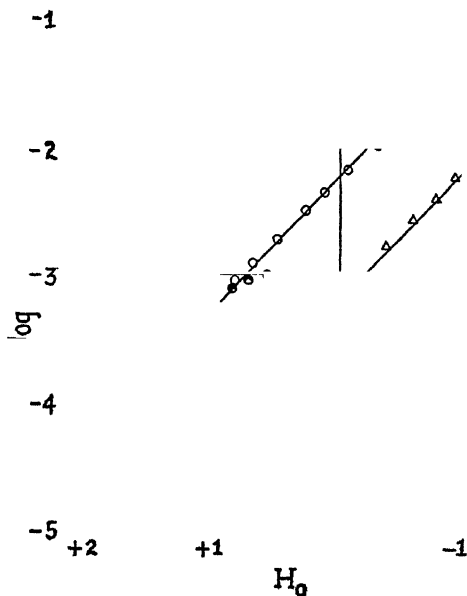


FIG. 4. Relation between H_0 and velocity constants for hydrolysis of ethyl acetate and for hydrolysis of cyanamide. Ethyl acetate hydrolysis: ○, 0.01-1.50 M HCl ; ●, 0.1 N HCl + 0-3 M KCl . Cyanamide hydrolysis: △, 0.05-5.0 M HNO_3 ; ▲, 0.25 N HNO_3 + 0-2.7 M KNO_3 .

Thus curve A in figure 5 shows an excellent agreement between the reaction rate data of Lobry de Bruyn and Sluiter (7, 18) for the Beckmann rearrangement of acetophenone oxime and the acidity functions of the sulfuric acid-water mixtures of concentrations from 93.6 to 98.7 per cent in which the reaction was carried out. The fundamental similarity of this reaction to an acid catalysis in dilute aqueous solution which is suggested by this result is of especial interest, because sulfuric acid-water mixtures of proper concentration have recently been shown to be excellent preparative reagents for this reaction (24).

Curve B in the same figure shows similar agreement with the acidity

function for the data of DeRight (10) on the rate of decomposition of formic acid into carbon monoxide and water. The marked inhibition by small amounts of water of the rate of this and similar reactions in concentrated sulfuric acid has long been a matter of interest. The present result shows that it may be treated quantitatively as the inhibition by a base of an acid-catalyzed reaction; that it is the same sort of thing as the inhibition by sodium hydroxide of the hydrochloric acid-catalyzed hydrolysis of sucrose or ethyl acetate.

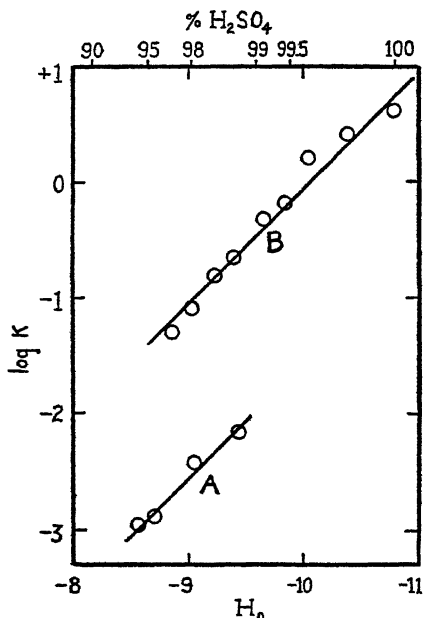
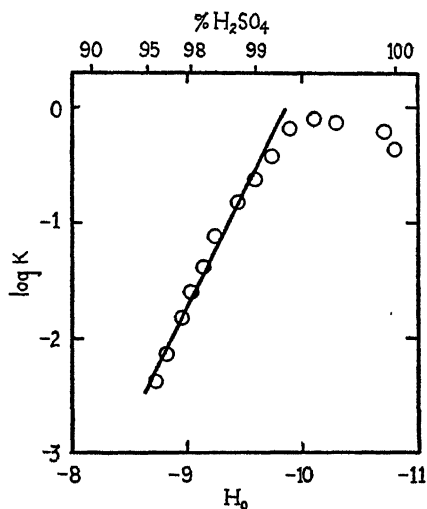


Fig. 5. Relation between H_0 and velocity constants for (A) Beckmann rearrangements of acetophenone oxime, (B) formic acid decomposition

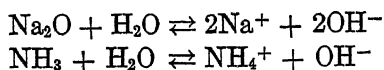
The reaction rate data of Wiig (27) on the decomposition of citric acid offers a somewhat more complicated picture (figure 6). Over a large part of the range studied, there is agreement with a straight line of slope -2 , but at very high acidities wide deviations appear and the actual curve goes through a maximum. In the region of the straight line, the reaction is clearly analogous to one in dilute aqueous solution whose rate is proportional to the square rather than to the first power of the hydrogen-ion concentration, certainly a conceivable situation. And the phenomenon of a maximum at a particular acidity, on both sides of which the rate drops off, is not infrequently found among acid-catalyzed reactions in dilute aqueous

solutions (8, 9). In both aqueous and sulfuric acid media detailed explanations for the appearance of the maximum can easily be found. Thus citric acid is very probably a polyacid base which can form several ions of differing charge by the addition of different numbers of hydrogen ions. To account for the maximum it is only necessary to suppose that some particular ion is more reactive than the product which is formed from it by the addition of further hydrogen ion. To make this picture more than a mere speculation will, however, require further information on the state of citric acid in solution in sulfuric acid.

The decompositions of formic and citric acids are typical of a number of decomposition reactions which take place in concentrated sulfuric acid



reactions which are the exact analogues of the reactions of sodium oxide and of ammonia with water.



Furthermore the data of Whitford (26) and of Dittmar (12) on the decomposition of malic and of triphenylacetic acids show that, in nearly every case, the inhibiting effect is the same per mole of bisulfate ion with these other inhibitors as it is with water.³ Now bisulfate ion plays the same part in sulfuric acid as hydroxyl ion does in water, and its concentration bears the same inverse relation to the acidity function in sulfuric acid that the concentration of hydroxyl ion does to the pH in water. The exact analogue in aqueous solutions of these reactions would therefore be a reaction which takes place in an alkaline medium at a rate which increases with decreasing pH. An example of this situation may be found in the polymerization of cyanamide in strongly alkaline solutions. Buchanan and Barsky (8) found that under these conditions the rate increases with decreasing alkalinity, and that it may therefore be said to be acid-catalyzed in spite of the high alkalinity of the medium. This reaction also exhibits a maximum at a particular pH and thus shows a close, although a purely formal, similarity to the decomposition of citric acid in sulfuric acid.

This group of acid decompositions represents only part of a much larger classification of reactions in which a molecule of water is split out from one or more molecules of reactants and in which sulfuric acid, concentrated hydrochloric acid, zinc chloride, or the like are commonly used as condensing agents. This includes such familiar reactions as nitration, the preparation of ethers and ethylene derivatives from alcohols, and many nuclear condensations, both intra- and inter-molecular, of which the anthraquinone synthesis from benzoylbenzoic acid and reactions used in the preparation of triphenylmethane dyes are important examples. It has been rather generally supposed that the function of the condensing agent is really that of a dehydrating agent, which by combination with the water formed in the reaction is able somehow to accelerate it. The reasoning back of this idea is not particularly sound, but the best evidence that the explanation is an entirely unsatisfactory one is the frequency with which it has been reported with a note of surprise that the much more efficient dehydrating agent phosphorus pentoxide has been found to be quite useless as a condensing agent in a reaction in which sulfuric acid is very effective.

On the other hand, the hypothesis that the reactions are acid-catalyzed,

³ This fact was obscured in the papers referred to because the molar concentrations of the inorganic bisulfates were calculated in terms of neutral sulfates.

that the function of the condensing agent is to provide a medium of sufficiently high acidity, agrees with all of the rather qualitative information available.⁴ It predicts that phosphorus pentoxide should not be an effective condensing agent, and it further predicts that other condensing agents are to be sought among strongly acidic media. Upon the success of the latter prediction must depend the ultimate judgment as to its validity.

REFERENCES

- (1) BREDIG AND LICHTY: *Z. Elektrochem.* **12**, 459 (1906).
- (2) BRÖNSTED: *J. Chem. Soc.* **119**, 574 (1921).
- (3) BRÖNSTED: *Chem. Rev.* **5**, 231 (1928).
- (4) BRÖNSTED: *Z. physik. Chem.* **169**, 52 (1934).
- (5) BRÖNSTED, DELBANCO, AND TOVERG-JENSEN: *Z. physik. Chem.* **169**, 361 (1934).
- (6) BRÖNSTED AND PEDERSEN: *Z. physik. Chem.* **108**, 185 (1924).
- (7) DE BRUYN, LOBRY, AND SLUITER: *Kgl. akad. wetenschappen, afdeling der wis- en natuurkund* **13**, 813 (1904).
- (8) BUCHANAN AND BARSKY: *J. Am. Chem. Soc.* **52**, 195 (1930).
- (9) CONANT AND BARTLETT: *J. Am. Chem. Soc.* **54**, 2881 (1932).
- (10) DERIGHT: *J. Am. Chem. Soc.* **55**, 4761 (1933).
- (11) DERIGHT: *J. Am. Chem. Soc.* **56**, 618 (1934).
- (12) DITTMAR: *J. Phys. Chem.* **33**, 533 (1929).
- (13) DITTMAR: *J. Am. Chem. Soc.* **52**, 2746 (1930).
- (14) GLEASON AND DOUGHERTY: *J. Am. Chem. Soc.* **51**, 310 (1929).
- (15) HALFORD: *J. Am. Chem. Soc.* **55**, 2272 (1933).
- (16) HAMMETT: *J. Am. Chem. Soc.* **50**, 2666 (1928).
- (17) HAMMETT: *Chem. Rev.* **13**, 61 (1933).
- (18) HAMMETT AND DEYRUP: *J. Am. Chem. Soc.* **54**, 2721 (1932).
- (19) HAMMETT AND DEYRUP: *J. Am. Chem. Soc.* **55**, 1900 (1933).
- (20) HAMMETT AND DIETZ: *J. Am. Chem. Soc.* **52**, 4795 (1930).
- (21) HAMMETT AND PAUL: *J. Am. Chem. Soc.* **56**, 827 (1934).
- (22) HAMMETT AND PAUL: *J. Am. Chem. Soc.* **56**, 830 (1934).
- (23) HANTZSCH: *Z. Elektrochem.* **29**, 221 (1923).
- (24) HILDEBRAND: Thesis, Columbia University, 1933.
- (25) LICHTY: *J. Phys. Chem.* **11**, 225 (1907).
- (26) WHITFORD: *J. Am. Chem. Soc.* **47**, 953 (1925).
- (27) WIIG: *J. Am. Chem. Soc.* **52**, 4729 (1930).
- (28) WIIG: *J. Am. Chem. Soc.* **52**, 4737 (1930).

⁴ The quantitative relation between rate and acidity function previously noted (18) in the case of the anthraquinone synthesis from benzoylbenzoic acid was based upon an error in figure 1 of the article by Gleason and Dougherty (14). Professor Dougherty has kindly informed me that the ordinates given in that figure should be increased by 10 to obtain the true values. With these corrected values an approximate relation is obtained, which is perhaps as good as is to be expected in view of the difference in the temperatures at which the rate and the indicator measurements were made, and because the large concentrations of benzoylbenzoic acid, itself a base, make the acidity of the reaction mixture differ from that of the sulfuric acid-water mixture in which it was dissolved. Further experimental data which avoids these difficulties is obviously needed.

NEW INDICATORS FOR OXIDIMETRY

GEORGE H. WALDEN, JR.

Department of Chemistry, Columbia University, New York City

AND

SYLVAN M. EDMONDS

Department of Chemistry, College of the City of New York, New York City

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Among the numerous oxidation potential indicators which have been reported, few have had any application to that important branch of oxidimetry which involves strong oxidants. For such use an indicator must have, in addition to the general properties of a good indicator, a high resistance to destruction by irreversible oxidation at high potentials. Otherwise it can only be used when the standard reagent is the oxidizing reagent; back-titration is impossible, and even in the forward titration the indicator is partly destroyed in the regions of local excess and the end point is fleeting. With the noteworthy exception of diphenylamine and its sulfonic acid (3, 4, 5, 6, 7), all oxidation potential indicators that have been reported prior to those which are the subject matter of this paper are so deficient in this important respect that their usefulness is very limited. In addition to this difficulty, there has been an almost complete lack of indicators with color changes in the higher oxidation potential region. Diphenylamine-sulfonic acid changes color at the highest potential,—0.83 to 0.84 volt in sulfuric acid solution against the normal hydrogen electrode (6). This is too low for many titrations, including the very important titration of ferrous iron in the absence of phosphoric acid or fluoride ion.

PHENANTHROLINE-FERROUS ION INDICATOR

The complex ferrous ions of α, α' -dipyridyl and *o*-phenanthroline were discovered and described by Blau (1) in 1898. These ions are readily formed by dissolving the nitrogen base in a nearly neutral water solution of ferrous sulfate. Both possess brilliant red colors, quite similar in quality, and of dye intensity. They are oxidized only by very strong oxidizing agents to substances of a pale blue color. Blau showed that the ferrous complexes were composed of one mole of ferrous ion combined with three moles of the nitrogen base, and that the oxidation process was the

simple conversion to the corresponding ferric complex ion without change of composition. The reaction has been found to be rapid and reversible (8, 10). Moreover the complexes are almost completely resistant to any further oxidation. This resistance is so marked that even acid permanganate solution does not attack them with appreciable rapidity at room temperature. The color change in both cases is completely reversible and of a vividness equal to that of phenolphthalein. In the presence of strong acids both complexes dissociate, but at very different rates, the dissociation of the phenanthroline complex being much the slower.

Attempts to measure the oxidation potential of the reactions by means of titration curves met with good success in the case of the phenanthroline complex, but yielded only very approximate results with the dipyridyl complex. The difficulty is undoubtedly due to the more rapid dissociation of the latter substance. About all that could be learned from the very erratic data obtained was that the oxidation potential could not be greatly different from that of the phenanthroline reaction. This is further borne out by the behavior of this substance when used as a titration indicator. From the excellent titration curves obtained with the phenanthroline complex it was calculated that the normal oxidation potential of the reaction



in 1 *M* sulfuric acid is 1.14 volts against the normal hydrogen electrode.

Because of the superior stability of the phenanthroline complex, its application as a titration indicator has been studied exclusively. The red color of the ferrous complex is sufficiently vivid so that one drop of 0.025 *M* solution in a volume of 200 cc. gives about the optimum color intensity for this use. When completely oxidized the much less intense blue color of the ferric complex is completely invisible. It therefore functions as a one-color indicator, with the threshold of visibility at about 90 per cent oxidation. The effective oxidation potential of the indicator is therefore about 1.20 volts against the normal hydrogen electrode. This potential is high enough to give a correct end point when iron or even considerably stronger oxidizing agents are titrated. In fact, if the potential were any higher the indicator could not be used for precise titrations with ceric sulfate.

A number of analytical applications have been studied. The indicator has been found to function excellently in simple titrations with solutions of ceric sulfate and potassium dichromate. In a more complicated setting (9, 11) it has been found that in a 5 *M* sulfuric acid solution containing both iron and vanadium, the color change occurs at a potential where iron is completely oxidized, but vanadium is only oxidized to the quadrivalent state. At lower acidities the color change occurs only after both sub-

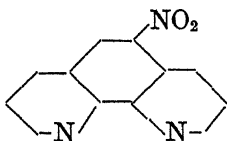
stances are completely oxidized. Very good methods of determining iron and vanadium in the presence of each other and of many normally interfering substances have been worked out.

OTHER INDICATORS OF THE PHENANTHROLINE-FERROUS ION GROUP

The highly desirable properties of phenanthroline-ferrous ion indicator have induced us to search for other indicators of the same type. Our work (2) has been along two lines: the study of other metallic complexes of phenanthroline—Blau described several—and the study of ferrous complexes of nitrogen bases related to phenanthroline.

Investigation of other metallic complexes of phenanthroline has failed to disclose another indicator, although the cobaltous and chromous complexes have interesting properties. They do not, however, possess sufficiently vivid colors.

The preparation of phenanthroline derivatives was at first hampered greatly because of the difficulty and expense of obtaining phenanthroline in quantity sufficient for preparative work. Now that this substance has been made commercially available we expect that this work will be greatly accelerated. Up to the present time we have studied only one such substance. This is a nitration product of phenanthroline, which, from its method of preparation and combustion analysis we judge to be the mono-nitro derivative



This compound forms a complex ion with ferrous ion, with color properties very similar to the phenanthroline complex. But unlike phenanthroline the complex forms in the presence of considerable concentrations of strong acid. It is oxidized to the same sort of a blue compound, presumably the corresponding ferric ion. We have not been able to make an experimental titration curve. From the behavior of the system when this is attempted we have concluded that this ferric ion is quite unstable. When it is attempted to use this indicator for the titration of iron with ceric sulfate the end point is appreciably late, showing that the oxidation potential is too high for the titration. From the amount of overtitration required to produce the color change we have calculated that the effective oxidation potential must be as high as 1.25 volts in 1 *M* sulfuric acid against the normal hydrogen electrode. This result is extremely interesting, because it shows that the oxidation potential of the ion has been changed by substi-

tution in the organic part. Since there are a large number of such derivatives it seems probable that other indicators of this type will be found, with, we may reasonably hope, oxidation potentials covering a considerable range.

DIPHENYLAMINE DERIVATIVES

We have also investigated the indicator properties of a number of diphenylamine derivatives. The effects of substituting nitro and amino groups were studied.

p-Nitrodiphenylamine is oxidized by strong oxidizing agents to an intensely reddish-violet compound. As an indicator it exhibits most of the peculiarities of diphenylaminesulfonic acid, but is somewhat more reversible. Its oxidation potential is about 0.2 volt higher than that of diphenylaminesulfonic acid. This is high enough so that it serves for the direct titration of iron with ceric sulfate in the absence of phosphoric acid. Results obtained with it for this titration compare very favorably with others obtained with phenanthroline-ferrous ion. It is not sufficiently immune to further oxidation to allow ceric sulfate to be titrated with ferrous sulfate. Nor does it function well when iron is titrated with potassium dichromate, owing to slow reaction. While thus not as good in general as phenanthroline-ferrous ion, it is a much cheaper material and is, within its limitations, an excellent indicator.

All of the six dinitro derivatives which we have studied show no color change even when treated with ceric or permanganate ions or with sodium bismuthate in acid solution; apparently the oxidation potential required is raised so much by the second nitro group that these powerful oxidizing agents are incapable of producing the reaction.

p-Aminodiphenylamine can be oxidized to a reddish-violet compound which can be reversibly reduced to a colorless compound. It is so easily destroyed by the action of excess oxidant that it is not satisfactory as an indicator. It is of interest, however, because its oxidation potential is lower than that of diphenylamine. It was not possible to measure its oxidation potential precisely, owing to the instability of the compound, but it is apparently somewhat below the ferrous-ferric ion potential in 1 *M* sulfuric acid. *p*-Acetylaminodiphenylamine is oxidized by ceric sulfate to a greenish-blue compound which is somewhat more resistant to further oxidation than is the colored compound from the non-acetylated derivative, but still not sufficiently so to be of much use. Its oxidation potential appears to be about 0.06 volt below the ferrous-ferric potential in 1 *M* sulfuric acid.

Strangely enough, 2,4-diaminodiphenylamine is an excellent indicator, quite free from the defects of destruction by excess oxidant. The colored

oxidation product is red, and it is only very slowly destroyed by excess ceric sulfate. The reversibility of the reaction is so good that we were able to make quite good titration curves, both for the oxidation with ceric sulfate and for the reduction with titanous chloride. While these two curves do not agree perfectly, they are good enough to show that both the oxidation and reduction are divalent, and that the oxidation potential in 1 *M* sulfuric acid is 0.70 volt against the normal hydrogen electrode. An indicator in this range, stable toward strong oxidizing agents and strong acids, has not been previously reported.

We have also studied a number of other polyamino derivatives of diphenylamine, but our work has yielded nothing of further interest. Some of these compounds are similar in oxidation potential and behavior to 2,4-diaminodiphenylamine; others are easily destroyed by excess oxidant. The reduction products from 2,4,6-trinitrodiphenylamine and from 2,4,6,3'-tetranitrodiphenylamine show no indicator properties whatever with ceric sulfate.

REFERENCES

- (1) BLAU: *Monatsh.* **10**, 372 (1889); **19**, 647 (1898).
- (2) HAMMETT, WALDEN, AND EDMONDS: *J. Am. Chem. Soc.* **56**, 1092 (1934).
- (3) KNOP: *J. Am. Chem. Soc.* **46**, 263 (1924).
- (4) KOLTHOFF AND SARVER: *J. Am. Chem. Soc.* **52**, 4179 (1930).
- (5) SARVER: *J. Am. Chem. Soc.* **49**, 1472 (1927).
- (6) SARVER AND KOLTHOFF: *J. Am. Chem. Soc.* **53**, 2902 (1931).
- (7) SCHOLLENBERGER: *J. Am. Chem. Soc.* **53**, 88 (1931).
- (8) WALDEN, HAMMETT, AND CHAPMAN: *J. Am. Chem. Soc.* **55**, 2649 (1933).
- (9) WALDEN, HAMMETT, AND EDMONDS: *J. Am. Chem. Soc.* **56**, 57, 350 (1934).
- (10) WILLARD AND YOUNG: *J. Am. Chem. Soc.* **55**, 3260 (1933).
- (11) WILLARD AND YOUNG: *Ind. Eng. Chem., Anal. Ed.* **6**, 48 (1934).

ADSORPTION INDICATORS

I. M. KOLTHOFF

School of Chemistry, University of Minnesota, Minneapolis, Minnesota

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MECHANISM OF THE INDICATOR ACTION

As was first shown by A. Lottermoser (18, 19), the silver halides acquire a positive charge if the supernatant liquid contains an excess of silver salt, and a negative charge if the liquid contains the halide ion in excess. Silver bromide, for example, in contact with a solution containing an excess of silver nitrate fixes (adsorbs) silver ions on its surface, thus acquiring a positive charge. In the immediate neighborhood of the adsorbed silver ions an equivalent number of anions—in this case nitrate ions—must be adsorbed in order to maintain the electroneutrality of both liquid and solid phases. There is, therefore, a primary adsorption of silver ions and a secondary adsorption of foreign anions. Any anion of a dissolved silver salt when shaken with the silver bromide will be dragged to the surface by the adsorbed silver ions. According to the so-called Paneth-Fajans-Otto Hahn adsorption rule the adsorbability of the anion increases as a first approximation, with decreasing solubility of its silver salt and increasing deformability of the anions. The large organic dye ions—especially those of the fluorescein series—distinguish themselves by being easily deformable by silver ions in the adsorbed state and by the fairly slight solubility of their silver salts. These dyes, therefore, are strongly adsorbed by the silver halides, and give rise to the formation of an intensely colored adsorption layer.

The use of dyestuffs as indicators in precipitation analysis originated with K. Fajans (3, 4, 5, 6) and his collaborators. Since the color change at the end point is caused by an adsorption process, Kolthoff (9) coined the term "adsorption indicators." The principle on which the functioning of an adsorption indicator is based is clearly demonstrated by a simple experiment (2).

Take a liter of an aqueous solution of the sodium salt of eosin containing about 3 mg. of the salt. The latter is dissociated and partly hydrolyzed, and the solution shows the characteristic greenish fluorescence as well as a yellowish red color in transmitted light. Upon the addition of 2 cc. of 0.1

N silver nitrate solution, no appreciable change in the color takes place because the solubility product of the silver salt of eosin is not exceeded. If 0.5 cc. of 0.1 *N* alkali bromide solution is now added, an intense color change to red or red-violet occurs and the fluorescence decreases. The silver bromide formed is very finely divided and adsorbs silver ions which are present in excess in the solution. Simultaneously an equivalent number of eosin ions are adsorbed at the surface of the silver bromide particles, whereby the dye ions are deformed, the process being accompanied by an intense change of the color to red. On further careful addition of bromide, more silver bromide is formed and the color of the suspension deepens, until the equivalence point is passed. At this point all the adsorbed silver is removed from the surface and the adsorbed eosin ions return to the solution. The silver bromide particles are thereby decolorized, and the solution regains its yellowish red color and fluorescence. As soon as the solution contains an excess of bromide ions the latter will be primarily adsorbed and the eosin will remain in the solution. The color change is reversible.

Instead of working with an acid dye it is also possible to use a suitable dye cation as an adsorption indicator. The order of the color change is then just the reverse of that described in the above example. If a few drops of a dilute solution of the basic dye, Rhodamine 6G, are added to a silver solution, the color does not change upon careful addition of bromide. The silver ions are primarily adsorbed and prevent the adsorption of the dye cations. As soon as all the silver is precipitated and a slight excess of bromide is present, the bromide ions are adsorbed, and attract an equivalent amount of dye cations to the surface, resulting in an intense color change of the suspension to red.

The classical interpretation (3, 4, 5, 6) of the adsorption indicator mechanism therefore is as follows: A dye anion is not adsorbed by a silver halide as long as halide ions are present in excess in the supernatant liquid. With a slight excess of silver ions part of the latter are adsorbed by the silver halide, which results in an equivalent adsorption of the dye anions. The reverse is true with a dye cation as adsorption indicator. The adsorption of the dye is usually accompanied by an intense color change, which indicates the equivalence point. Although very desirable, it is not strictly necessary that a change in color shall occur at the end point. As long as the indicator is in the unadsorbed state the supernatant liquid shows the color of the dissolved dye and the precipitate is white (silver chloride) or yellowish (silver bromide and iodide); when the strong adsorption of the dye takes place the supernatant liquid is decolorized and the precipitate assumes the color of the adsorbed dye. Berry and Durrant (1) made use of this fact in the application of tartrazin as an indicator in the titration of silver with bromide or chloride. The precipitate has a yellow color as long

as there is an excess of silver in the solution; at the end point the dye is replaced by halide ions and goes into solution, imparting a yellowish green color to the latter. According to my experience the method gives satisfactory results, but one must titrate very carefully, since the color change is not strictly reversible. The use of diphenylamine blue (oxidized diphenylamine) by Lang and Messinger (17) for the titration of strongly acid chloride solutions with silver nitrate is based on the same principle. The basic dye is adsorbed with a green color in the presence of an excess of chloride and the solution is colorless; at the end point a desorption occurs and the solution becomes violet. If the titration is performed carefully, satisfactory results are obtained with 0.02 to 0.1 *N* chloride solutions; with 0.01 *N* or more dilute solutions, however, I obtained a vague end point which occurred too late.

Upon closer examination it appears that the classical interpretation of the mechanism of the adsorption indicator action is not entirely adequate to explain the experimental facts. A dye anion should not be adsorbed when there is an excess of halide in the solution, but should be dragged to the surface with silver ions when the latter are in excess. The reverse should be true for a dye cation. However, various cases are known in which an adsorption of a dye anion occurs when there is an excess of halide ion in the solution. Eosin, for example, cannot be used as an adsorption indicator in the titration of chloride; the dye ions are strongly adsorbed by the suspended particles from the very beginning of the titration, in spite of the presence of a large excess of chloride ions. Therefore no pronounced color change is noticeable at the end point, although the adsorption of the eosin increases with an excess of silver and decreases with increasing amounts of chloride. But even with indicators which are quite useful for the detection of the end point, a similar behavior is generally noticed. For example, phenosafranine—a basic dye—is quite useful in the titration of silver with bromide. Still a slight adsorption of the dye takes place when silver ions are in excess, the adsorption increasing with decreasing silver-ion concentration. At the equivalence point, and especially with a slight excess of bromide, a sudden increase of the adsorption of the dye occurs and a distinct color change is observed. The case is also clearly demonstrated by the behavior of methyl violet—a basic dye—in the titration of silver with chloride (7). In weakly acid medium with an excess of silver ions the suspension in the presence of the dye has a greenish color (in neutral medium, blue); with an excess of chloride ions all the dye is adsorbed on the particles, imparting a pink color to the latter. However, a marked adsorption of the dye occurs even when silver ions are still in excess. Hodakow titrated a mixture of 8 cc. of 0.02 *N* silver nitrate and 5 cc. of a 0.004 per cent methyl violet solution with 0.02 *N* sodium chloride

and determined the amounts of dye adsorbed at various stages during the titration. In figure 1 the percentage of dye adsorbed (ordinate) is plotted against the excess of silver and chloride respectively in the neighborhood of the equivalence point. There is a sudden increase in the amount of methyl violet adsorbed at the equivalence point, the adsorption curve resembling a potentiometric titration curve. The smaller the amount of indicator used the more pronounced is the inflection at the equivalence point.

The above phenomenon, of a dye being already markedly adsorbed in the presence of a lattice ion of the same electrical charge, is not easily

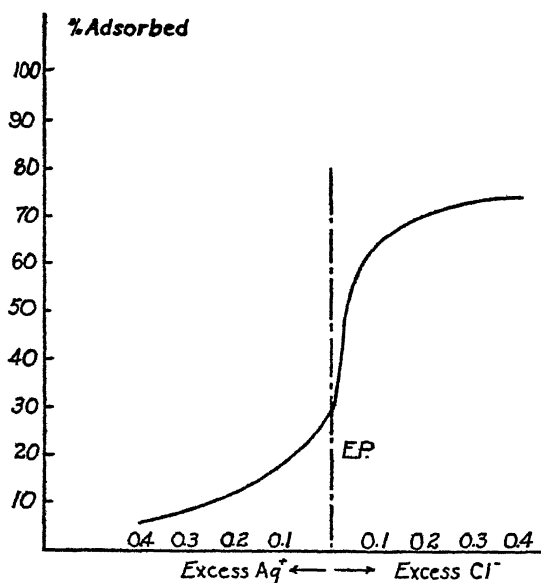
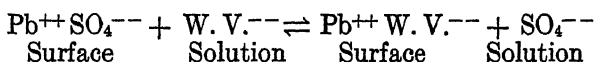


FIG. 1. Adsorption of methyl violet by silver chloride

explained on a classical basis. In the first place it should be clearly understood that the indicator action is attributed to a secondary adsorption of the dye, the lattice ion of opposite sign being primarily adsorbed. If, on the other hand, the dye is adsorbed when there is an excess of lattice ions of the same sign in solution, on the classical basis we should be forced to infer that in the latter condition a primary adsorption of dye ions occurs. A silver halide, for example, adsorbs its own ions preferentially and is thereby peptized. This adsorption is supposed to take place at active spots on the surface. It cannot be expected that the large dye ions, which do not fit in the lattice of the silver halide, can replace the halide or silver ions at the active spots. If this were true, one would expect that dye ions,

which exert such a strong replacing effect upon adsorbed lattice ions of the same electrical charge, should exert at least as strong a peptizing effect upon the particles of the precipitate as the lattice ions do. This is contrary to the behavior of colloidal solutions¹ (16).

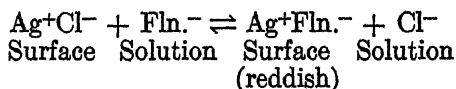
The fact that dye ions can be adsorbed although an excess of lattice ions of the same sign is in the solution, indicates that we are dealing here with an exchange adsorption, involving dye ions and lattice ions of the same sign, in the surface of the particles. Such an exchange was first described by Kolthoff and Rosenblum (12) and has been substantiated by experiments of Kolthoff and Sandell (13) and of von Fischer and Ch. Rosenblum (14). If well-aged lead sulfate, for example, is shaken with a wool violet solution, the dye ions exchange with sulfate ions on the surface of the lead sulfate:



There is a competition between wool violet and sulfate ions to be fixed on the surface of the lead sulfate. An excess of lead ions in the solution favors the adsorption of the dye, and an excess of sulfate ions naturally promotes the adsorption of the latter at the expense of the dye. The general shape of the adsorption curve of wool violet by lead sulfate therefore resembles that of an adsorption indicator which is adsorbed at both sides of the equivalence point (figure 1).

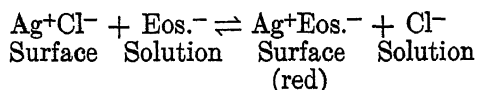
The behavior of adsorption indicators is then easily explained on the basis of an exchange adsorption between lattice ions and dye ions of the same sign at the surface of the particles.

If silver chloride which does not contain either an excess of adsorbed silver or of adsorbed chloride (equivalent body) is shaken with a solution of the sodium salt of fluorescein (Fln.⁻), a slight adsorption of the latter takes place, and an equivalent amount of chloride ions



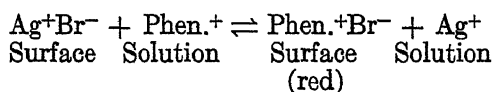
¹ Actually a positively charged sol shows very small flocculation values with suitable acid dyes, and negatively charged sols are easily flocculated by suitable basic dyes. This shows that the secondary adsorption at active spots is very pronounced and results in the destruction of a double layer. It is possible that an excess of dye will replace lattice ions of the same sign in the surface of the particles. The chemical composition of the surface layer is then entirely changed, and it is quite possible that an excess of dye may peptize the particles again, since the dye ion in the solution is identical with that fixed in the surface layer. This would explain the occurrence of the so-called "irregular series" in colloid chemistry. This point will be further tested experimentally.

are sent into solution. In this particular case there is only a slight replacement of chloride ions by fluorescein ions; in the presence of a slight excess of silver, however, the chloride-ion concentration decreases sharply, favoring a marked replacement of chloride ions in the surface by dye ions, resulting in a reddish coloration of the precipitate. Fluorescein therefore is a very suitable adsorption indicator in the titration of chloride. Eosin, on the other hand, cannot be used for this purpose, since it is adsorbed much more strongly than fluorescein ions. If an equivalent body of silver chloride is shaken with an eosin solution the precipitate is strongly colored:



The adsorption of eosin is favored by an excess of silver and is decreased by an excess of chloride. The dye is a very suitable indicator for the titration of bromide and iodide, as is easily understood by the above interpretation.

The behavior of basic dyes as adsorption indicators is similar to that of acid dyes. The basic dye competes with the silver ion in being adsorbed at the surface of the silver halide. If phenosafranine (a basic dye) is shaken with silver bromide a slight exchange takes place:



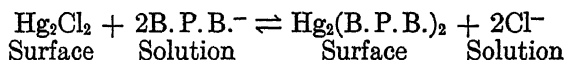
An excess of silver ions decreases this adsorption very strongly; an excess of bromide ions favors the exchange, resulting in a marked deepening of the color of the precipitate. In our interpretation, therefore, we do attribute the color change not to a secondary adsorption of the dye at active spots (Fajans et al. (3, 4, 5, 6)), but to an exchange adsorption involving lattice ions and dye ions of the same electrical sign on the entire surface of the precipitate. The secondary adsorption may be partly responsible for the color change, but does not explain why the dye is adsorbed when there is still an excess of lattice ions of the same sign as that of the indicator ions in the solution.

In the titration of chloride with fluorescein, a striking change in the appearance of the precipitate occurs at the point of distinct color change. The flocculent precipitate suddenly becomes grainy and consists of a large number of red globular particles. At this point the composition of the surface layer of the particles partly changes from silver chloride into silver fluoresceinate.

Another phenomenon in harmony with our interpretation is the fact

that the adsorption of a suitable dye by freshly formed silver chloride does not change with long periods of shaking. If the dye is added at various time intervals after the precipitation of the silver chloride, its adsorption decreases very rapidly. The adsorbed dye therefore protects the fresh precipitate from aging (agglomeration of the particles), a phenomenon similar to the inhibition of recrystallization of lead sulfate by adsorbed wool violet (14).

Experiments were performed to substantiate the above view of the mechanism of the action of adsorption indicators. In a study with W. Larson—details of which are to be published later—of the titration of chlorides and bromides with mercurous nitrate, using various adsorption indicators, it appeared that bromophenol blue was very suitable. Chloride was titrated potentiometrically with the mercurous solution exactly to the equivalence point. Then a measured volume of bromophenol blue solution was added quickly, and the change of the potential observed. It appeared that when the precipitate became colored the change in potential indicated the formation of an excess of chloride in the solution.



Experiments were also made with freshly precipitated silver chloride. The supernatant liquid, containing an excess of silver, was poured off immediately after precipitation, and the precipitate was quickly washed until no silver could be detected in the wash water. The ten-minutes old washed precipitate was suspended in a little water, and the silver-ion concentration measured potentiometrically. The potential corresponded exactly to that of a saturated solution of silver chloride in water. From this measurement and from the change of the potential upon careful addition of 0.01 *N* sodium chloride solution, it could be definitely inferred that the washed precipitate did not contain any adsorbed silver salt. Washed precipitates prepared in a similar way were shaken for 2 minutes with 10 cc. of a 0.02 per cent solution of the sodium salt of fluorescein in water. The precipitate turned orange-pink; upon washing with water it remained pink and acquired a much more intensive color upon addition of some fluorescein with a few drops of silver nitrate. The fluorescein solution with which the precipitate had been shaken was filtered and acidified with sulfuric acid, and the fluorescein removed by extraction with ether. The remaining aqueous solution was tested with silver nitrate, and the turbidity compared with a blank from an identical volume of saturated silver chloride solution containing the same amount of dye which had been treated in a similar way. The turbidity obtained with the dye solution which had been shaken with the silver chloride (0.7 g.) was much stronger than that

of the blank. The result shows very definitely that chloride ions in the surface of the silver chloride had been replaced by fluorescein ions, thus causing an excess of chloride to be present in the solution. A much stronger effect is obtained if the sodium salt of eosin is used instead of fluorescein. The former dye is much more strongly adsorbed by silver chloride and gives a much more pronounced exchange.

INFLUENCE OF VARIOUS FACTORS UPON THE SUCCESSFUL APPLICATION OF ADSORPTION INDICATORS

1. Choice of indicator

In the first place an adsorption indicator should have the property of being strongly adsorbed at the equivalence point, or with the slightest trace of excess of lattice ion of opposite electrical sign, and not at all or only very slightly adsorbed in the presence of excess of the lattice ion of the same sign. In other words, the adsorption curve during the titration should have a shape somewhat similar to a potentiometric titration curve. Preferably the indicator in the adsorbed state should show a color distinctly different from that in the liquid phase. The light sensitivity of the silver halides is greatly increased by adsorbed dye. These titrations therefore should not be carried out in direct sunlight.

2. Size of the precipitate

Since the adsorption of the indicator is limited to the surface layer, successful results can be expected only when the precipitate formed has a large surface development. This is the case with the silver halides, mercurous chloride, and mercurous bromide. In the titration of halides with silver or mercurous nitrate, the slightly soluble halide stays in colloidal solution until near the end point, when flocculation occurs. As long as the particles stay in colloidal solution they do not agglomerate and they have a large surface development. After flocculation occurs a rapid aging takes place by the formation of agglomerates, resulting in a decrease of the total surface of the precipitate. This explains why the presence of flocculating electrolytes in the solution interferes with the sharpness of the titration (20). This is especially the case in the titration of bromides with eosin as indicator. In the absence of flocculating electrolytes a beautiful color change is found at the equivalence point, especially if the titration is made in the presence of acetic acid. If by the presence of electrolytes (especially cations of higher valence exert this effect) the silver bromide flocculates long before the equivalence point is reached, it is found that the precipitate is slightly colored, thus making the color deepening at the end point less intense. The color at the surface of the precipitate in the presence of

an excess of bromide must be attributed to an exchange between bromide and eosin ions on the surface of the silver bromide. This exchange is inhibited as long as the particles remain in colloidal solution and contain the peptizing bromide ions at active spots. This view is substantiated by the following experiments. Fifty cc. of 0.02 *N* potassium bromide solution was titrated in the presence of acetic acid with eosin as indicator. The precipitate remained in colloidal suspension until 9.9 cc. of 0.1 *N* silver nitrate had been added; at 10.00 cc. the entire precipitate was flocculated and had a marked red color. The experiment was repeated, but after adding 9.6 cc. of 0.1 *N* silver nitrate, 5 cc. of 1 *N* barium nitrate were added. The silver bromide flocculated immediately and had a salmon-pink color. The deepening of the color at the equivalence point was much less pronounced.

3. Influence of the hydrogen-ion concentration

In general, hydrogen ions exert a flocculating effect and therefore an excess of acid will interfere with the detection of the end point (compare section 2). In various cases the hydrogen ions exert a specific effect upon the indicator, and the titration may be rendered impossible even in very slightly acid medium. Fluorescein, for example, is a very weak acid having an ionization constant of the same order as that of phenolphthalein. Hydrogen ions will remove the indicator ions by the formation of undissociated fluorescein. The titration therefore must be carried out in neutral medium. If the ionization constant of the indicator is increased by the introduction of chlorine, the titration can be carried out in weakly acid medium. Thus Kolthoff, Lauer, and Sunde (11) prepared dichlorofluorescein and found it very useful for titration of chloride at a pH smaller than 4. Eosin and diiodofluorescein and various other acid dyes, such as bromophenol blue, chlorophenol red, and metanil yellow, can be used in very weakly acid medium.

4. Dilution of the halide to be titrated

Bromides and iodides can be titrated with eosin as indicator in solutions even more dilute than 0.001 *N*. The silver halides separate in a very finely divided form, and the indicator is strongly adsorbed. Chlorides, on the other hand, cannot be titrated with fluorescein as indicator at dilutions greater than 0.005 *N*. Since the solubility of the silver chloride is much greater than that of the bromide or iodide, it separates in a coarser form having a smaller surface. In addition the adsorbability of the fluorescein ion is much smaller than that of eosin. Dichlorofluorescein is more strongly adsorbed than fluorescein and can, therefore, be used for the titration of more dilute chloride solutions (0.001 *N*) (11).

5. Influence of organic solvents

Addition of organic solvents has two pronounced effects upon the titration: (a) The solubility of most inorganic precipitates is decreased by the addition of an organic solvent. The precipitate, therefore, will separate in a much finer form as a result of an increased supersaturation. This should have a favorable effect. (b) On the other hand, the adsorbability of the indicator ions is changed—as a rule decreased—by addition of an organic solvent to the aqueous phase.

At my request Henry Yutzy in this laboratory has made several experiments in which chloride was titrated with silver nitrate in mixtures of water, alcohol, and glacial acetic acid, using eosin as an indicator. Eosin, as we have seen, cannot be used for the chloride titration in purely aqueous medium. It appeared that chloride can be titrated with this indicator, if the medium at the end point contains 10 to 25 per cent of alcohol and approximately 30 per cent of acetic acid. Although of relatively little practical importance, the results show definitely that the organic solvents favor adsorption of the chloride ions at the surface of the silver chloride at the expense of the eosin. It may be expected that alcohol and organic solvents will have a favorable effect in those cases when the primary precipitate separates in a microcrystalline form, having a small surface. If good adsorption indicators could be found for barium sulfate, calcium oxalate, lead sulfate, etc., successful titrations probably could be made in the presence of alcohol.

As a matter of record it may be mentioned that Kolthoff and Willman (15) applied eosin as an indicator in the titration of bromide with silver in glacial acetic acid as a solvent.

6. Influence of the temperature

Increase of the temperature quite generally will have an unfavorable effect for the following reasons: (a) Usually the solubility of the precipitate increases with the temperature, and therefore it will separate in a coarser form than at low temperature. (b) The speed of aging, resulting in a decrease of the surface of the fresh precipitate, is much greater at higher temperature. (c) The adsorbability of the indicator ions, as a rule, decreases with increasing temperature.

7. Fractional separations

With suitable adsorption indicators and under the proper conditions it is possible to determine an ion in the presence of another which also yields a slightly soluble salt with the reagent. According to Fajans and Wolff (5), iodide can be titrated in the presence of chloride with diiodofluorescein,

dimethyl diiodofluorescein, and rose bengal as indicators. Kolthoff (8) titrated small amounts of iodide in the presence of much chloride by adding ammonium carbonate and using eosin as an indicator.

OTHER APPLICATIONS OF ADSORPTION INDICATORS

It is beyond the scope of this paper to discuss or review all volumetric procedures with adsorption indicators.² The most important applications are in the titration of halides with silver or mercurous mercury or the reverse processes. In other cases the working conditions are very limited. G. E. Noponen in this laboratory has investigated the titration of lead with potassium ferrocyanide, using sodium alizarinsulfonate as indicator; the end point was vague.

Slightly better results were obtained in the titration of lead with potassium chromate, using orthochrome T as indicator, but the method has little practical significance. The determination of lead with oxalate, in which eight different adsorption indicators were tried, was not very successful either.

In qualitative analysis adsorption indicators are sometimes advantageously applied in the detection of traces of elements. The detection and the colorimetric determination of magnesium with titan yellow, of beryllium with curcumin and 1, 2, 5, 8-oxyanthraquinone, of aluminum with the latter reagent and with alizarin, aurintricarboxylic acid, purpurin, etc., are based on this principle.

By its behavior as an adsorption indicator it can be determined whether a dissolved dye is present as a cation or an anion. It was found, for example (10), that methyl red in neutral medium (yellow color) is adsorbed in the red form by silver thiocyanate containing an excess of silver ions. The dye therefore is present in the anion form in the solution. In 1 *N* sulfuric acid, on the other hand, the dye is strongly adsorbed by a precipitate containing an excess of thiocyanate. In strongly acid medium, therefore, the dissolved methyl red is present in the cation form. In a similar way it can be shown that various sulfonphthaleins in strongly acid medium are mainly present as cations, and in weaker acid or neutral medium as anions.

SUMMARY

1. The mechanism of the action of an adsorption indicator is to be attributed to an exchange between dye ions and lattice ions of the same electrical sign in the surface of the precipitate.

* A complete review (up to 1929) is given in I. M. Kolthoff's *Volumetric Analysis*, Vol. II, translated by N. H. Furman. John Wiley and Sons, New York (1929).

2. The various factors affecting the successful application of adsorption indicators to volumetric procedures have been discussed.

3. Applications of adsorption indicators to the qualitative detection and colorimetric determination of traces of elements have been mentioned. By examining the behavior of dyestuffs as adsorption indicators, it is possible to decide whether they are present in the form of cations or of anions.

REFERENCES

- (1) BERRY, A. J., AND DURRANT, P. J.: *Analyst* **55**, 613 (1930).
- (2) Compare FAJANS, K.: *Radioelements and Isotopes; Chemical Forces and Optical Properties of Substances*, p. 96. McGraw-Hill Book Co., New York (1931).
- (3) FAJANS, K., AND HASSEL, O.: *Z. Elektrochem.* **29**, 495 (1923).
- (4) FAJANS, K., AND STEINER: *Z. physik. Chem.* **125**, 309 (1927).
- (5) FAJANS, K., AND WOLFF, H.: *Z. anorg. allgem. Chem.* **137**, 221 (1924).
- (6) HASSEL, O.: *Kolloid-Z.* **34**, 304 (1924).
- (7) HODAKOW, J.: *Z. physik. Chem.* **127**, 43 (1927); **129**, 128 (1927).
- (8) KOLTHOFF, I. M.: *Z. anal. Chem.* **70**, 395 (1927).
- (9) KOLTHOFF, I. M.: *Volumetric Analysis, Vol. I. Theoretical Principles*, translated by N. H. Furman, p. 111. John Wiley and Sons, New York (1928).
- (10) Compare KOLTHOFF, I. M.: *J. Phys. Chem.* **35**, 1433 (1931).
- (11) KOLTHOFF, I. M., LAUER, W. M., AND SUNDE, C. J.: *J. Am. Chem. Soc.* **51**, 3273 (1929).
- (12) KOLTHOFF, I. M., AND ROSENBLUM, C.: *J. Am. Chem. Soc.* **55**, 2665 (1933).
- (13) KOLTHOFF, I. M., AND SANDELL, E. B.: *J. Am. Chem. Soc.* **55**, 2170 (1933).
- (14) KOLTHOFF, I. M., VON FISCHER, WM., AND ROSENBLUM, C.: *J. Am. Chem. Soc.* **56**, 832 (1934).
- (15) KOLTHOFF, I. M., AND WILLMAN, A.: *J. Am. Chem. Soc.* **56**, 1014 (1934).
- (16) Compare KRUYT, H. R., AND VAN DER WILLIGEN, P. C.: *Z. physik. Chem.* **139A**, 53 (1928).
- (17) LANG, R., AND MESSINGER, J.: *Ber.* **63**, 1429 (1930).
- (18) LOTTERMOSER, A.: *J. prakt. Chem.* **72**, 39 (1905); **73**, 374 (1906).
- (19) LOTTERMOSER, A., AND ROTHE: *Z. physik. Chem.* **62**, 359 (1908).
- (20) Compare MENZEL, H.: *Z. Elektrochem.* **33**, 68 (1927).

RADIOACTIVE INDICATORS IN ANALYTICAL CHEMISTRY

CHARLES ROSENBLUM

School of Chemistry, University of Minnesota, Minneapolis, Minnesota

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Radioactive elements used simply as a tool in chemical and physical research have been called radioactive indicators¹ (23). Since this term first appeared in the literature, innumerable applications of these indicators have been made to various problems of chemistry, physics, medicine, and biology (30), until at present a voluminous literature exists to bear testimony concerning their usefulness. Among the problems which have been attacked with their aid are many of analytical chemical significance; it is here proposed to summarize these contributions.

Radioactive indicators are not indicators in the usual analytical sense of the word, there being no question of a visual change. Their particular value lies rather in the ease and accuracy with which they are detectable in submicroscopic quantities. Their detection and measurement is simply effected by the use of suitable electroscopes and electrometers, or by means of the photographic plate, all of which are extremely sensitive to the radiations from radioelements. The type of electroscope employed depends of course on the nature of the element involved, i.e., on whether it emits alpha particles, beta particles or gamma radiation. Details of construction of instruments, and methods of obtaining and measuring radioactive preparations must be omitted here. They can be found by consulting standard texts on radioactivity (17, 28) and the scientific periodical literature (22). The Lind interchangeable head electroscopes (16) are very satisfactory for measuring alpha and gamma radiations. Convenient beta-ray electroscopes of simple construction are described in the literature (17, 22, 28).

The elements most frequently used in the past as indicators are included in table 1, together with their characteristic radiation (27). They have been chosen for the ease with which they are obtained and measured. The rate of disintegration of radioelements imposes a serious restriction on their general usefulness, for only elements which decay relatively slowly during the course of a series of experiments may be used. It will be seen that all

¹ This definition does not include the use of radioelements as sources of radiation in nuclear disintegration experiments.

elements listed save thoron, which is never used alone, have a convenient half-life.

Applications to analytical chemistry have been of two general types. On the one hand attempts have been made to use radioelements for strictly analytical purposes such as microanalyses and solubility determinations. More frequent, however, has been their use in studies relating to the nature of analytical precipitates and involving such puzzling phenomena as co-precipitation and aging. Such investigations are of interest to the analytical chemist and will be briefly described. For a more exhaustive discussion, the original papers must be studied.

TABLE 1
Common radioactive indicators

RADIOELEMENT	RADIATION	COMMON ELEMENT	HALF LIFE*
UX ₁	Beta	Th	24.5 days
Ra	Alpha	Ra	1590.0 years
Rn	Alpha	Rn	3.825 days
Ra D	Beta	Pb	22.0 years
Ra E	Beta	Bi	4.9 days
Po	Alpha	Po	140.0 days
Ms TH ₂	Beta	Ac	6.13 hours
Rd Th	Alpha	Th	1.90 years
Th X	Alpha	Ra	3.64 days
Th B	Beta	Pb	10.6 hours
Th C	Alpha, beta	Bi	60.5 minutes
Tn	Alpha	Rn	54.5 seconds

* Reference 27.

ANALYTICAL APPLICATIONS

Microanalysis

The strictly analytical applications will first be considered. Whenever a radioactive substance is added to a solution containing a given amount of inactive common element with which it is isotopic, the mixture is chemically inseparable; and the activity of the radioelement in arbitrary units thereafter represents the given weight of the common element in all of its chemical reactions. If now a certain fraction, say half, of the element is removed from solution by precipitation or electrodeposition, the same portion of the radioelement is simultaneously removed. The radioelement therefore acts as an indicator for the inactive element.

In this manner, G. von Hevesy and R. Hobbie (34) have taken advantage of the isotopic relationship between radium D and lead to place a radio-metric control on a large series of microdeterminations of lead made in connection with a study (33) of the abundance of lead in rocks from various

sources. Their procedure involved the separation of traces of lead from the siliceous mass by the use of hydrofluoric acid, and the subsequent anodic deposition of PbO_2 , which was determined gravimetrically. They then performed the lead determination colorimetrically. The agreement being poor, a control on the completeness of recovery became imperative. This was done simply by the addition of a small quantity of radium D soon after removal of silica, and by subsequently determining the radioactivity of the deposited lead. Knowing both the total activity of the radium D added and the activity recovered by electrolysis, they calculated directly the percentage of total lead which succeeded in reaching the anode. Since this percentage corresponds to the weight of lead actually recovered, the total weight could easily be found by correcting for the deficiency in the radium D activity. Table 2 illustrates the data found and shows the agreement between the various methods of determining lead.

TABLE 2
Rock analyses with radiometric control

KIND OF ROCK	WEIGHT OF SAMPLE	Pb ON ANODE $\frac{\text{g Pb}}{\text{g. Rock}}$	COLORIMETRIC DETERMINATION $\frac{\text{g. Pb}}{\text{g. Rock}}$	PER CENT OF Ra D RECOVERED	Pb CONTENT CORRECTED $\frac{\text{g Pb}}{\text{g. Rock}}$
	<i>grams</i>				
Dunite.....	34 6180	32×10^{-6}	30×10^{-6}	71	42×10^{-6}
Lherzolite.....	24 6817	15×10^{-6}	13×10^{-6}	69	19×10^{-6}
Granite.....	48 0611	18×10^{-6}	16×10^{-6}	53	30×10^{-6}
Basalt.....	28.0984	4×10^{-6}	5×10^{-6}	100	4×10^{-6}
Kimberlite.....	33 0458	12×10^{-6}	11×10^{-6}	69	16×10^{-6}

A similar procedure is mentioned by A. von Grosse (31), who used uranium X_1 as an indicator for thorium in determining as little as 0.01 per cent in Katanga pitchblende. Such a procedure is equally applicable to the determinations of traces of bismuth and thallium, both of which possess radioactive isotopes.

R. Ehrenberg (2) has proposed numerous radiometric microanalytical procedures based upon a succession of reactions ending with an incomplete precipitation of radioactive lead nitrate (containing thorium B). All reactions are carried out in a microcentrifuge cup to permit the separation of solids as they are formed. Starting with a series of solutions of known ion concentration, Ehrenberg establishes an empirical "standardization" curve relating the initial concentration of a given ion to the quantity of the thorium B remaining in solution.² It should be emphasized that each ion requires an individual calibration curve, which will vary with the condi-

²The amount of thorium B is measured by the alpha- or beta-ray activity of thorium C after radioactive equilibrium is established.

tions prevailing during the analysis. The chloride-ion determination (3) will serve to illustrate the principle of the method. First a standardization curve was constructed in the region under investigation, say 1.8×10^{-3} to 5.4×10^{-3} mg. of chloride ion. To 0.15 cc. of chloride solutions of known concentrations were added successively 0.5 cc. of $10^{-3} N$ silver nitrate solution, 0.05 cc. of $10^{-2} N$ potassium chromate solution, and 1.0 cc. of $10^{-3} N$ radioactive lead nitrate solution, centrifuging after each precipitation; then 1.0 cc. of the supernatant liquid was removed for measurement in an electroscope. Tabulating the initial chloride content of the known solutions with the residual activities, expressed both in arbitrary units (discharge of electroscope in unit time) and as a percentage of a control solution containing no initial chloride, we obtain table 3. If now a solution containing an unknown chloride content were treated as described, and the residual activity amounted to 50 per cent of the control activity (i.e., 5000 arbitrary units), then by a simple interpolation it would be found that the unknown had contained 2.1×10^{-3} mg. of chloride ion.

TABLE 3
Chloride-ion standardization

CL ⁻ CONCENTRATION IN MILLIGRAMS	ACTIVITY IN ARBITRARY UNITS	PER CENT ACTIVITY LEFT
0	10,000	100.0
1.8×10^{-3}	5,113	51.1
3.6×10^{-3}	4,533	45.3
5.4×10^{-3}	3,910	39.1

Similar micromethods have been presented for the determination of many anions and cations as well as for organic nitrogen and carbon; and a sugar determination has also been developed. Recently A. Polessitsky (26) has employed radium as an indicator for barium in a modification of Ehrenberg's method, and has determined several milligrams of barium in the presence of large amounts of lead. However, in all of these cases an empirical curve must first be established in the particular concentration range under investigation. Frequently linear relationships are obtained, though it is clear that these curves have no theoretical significance. As yet, no rigid test has been made of their accuracy or applicability to conditions usually encountered in the laboratory. It is uncertain whether such empirical methods will ever be of great utility except in isolated cases.

Solubility determinations

Solubility determinations constituted one of the first uses of radioactive indicators. The basis of such determinations is again the chemical inseparability of isotopic mixtures. If a radioactive lead salt is precipitated

from a solution containing originally a given weight of lead associated with a known activity of radioactive isotope (RaD or ThB), then the solubility of the precipitate, in terms of lead ions, is given directly by the activity of the saturated solution. For example, F. Paneth and G. von Hevesy (23), using radium D, prepared a radioactive solution containing 9.69 mg. of lead chloride and possessing a beta-ray activity of 2030 arbitrary units, from which they precipitated active lead chromate by the addition of potassium chromate. Thereupon the insoluble salt was washed and a saturated solution prepared at 25°C. The beta-ray activity of the evaporation residue from 70 cc. of a saturated solution was 0.150 unit, indicating that $\frac{323.2}{278.1} \times 0.00969 \times \frac{1000}{70} \times \frac{0.150}{2030} = 1.2 \times 10^{-5}$ g. of lead chromate or 0.4×10^{-7} mole was dissolved per liter. Later experiments by G. von Hevesy and E. Róna (35), using thorium B, raised this low value to 2×10^{-7} mole per liter, in good agreement with the average of values obtained by other methods. Unfortunately this procedure, until fairly recently, has not been further developed. At present, however, experiments are planned in which the solubility of lead salts as a function of particle size will be measured by the indicator method.

Recently we have made use of the Paneth specific surface determination (20, 25) to permit estimates of solubilities in regions difficult to investigate. From a study of the thorium B adsorption, Paneth has calculated the surface extent of samples of lead sulfate to be

$$\text{Specific surface} = \frac{\text{Pb}_{\text{surf.}}}{1 \text{ g. PbSO}_4} = \frac{\text{ThB}_{\text{surf.}}}{\text{ThB}_{\text{soln.}}} \times \frac{\text{Pb}_{\text{soln.}}}{\text{wt. of PbSO}_4}$$

where $\text{Pb}_{\text{surf.}}$ is the weight (or number of ions) of lead present in the outermost crystal layer, $\text{Pb}_{\text{soln.}}$ is the amount of lead in the given volume of solution, and the ratio $\frac{\text{ThB}_{\text{surf.}}}{\text{ThB}_{\text{soln.}}}$ is the ratio of adsorbed thorium B to that left in solution. Using a specified sample of lead sulfate and determining the thorium B adsorption in increasing concentrations of lead nitrate, it was found that the ratio $\frac{\text{ThB}_{\text{surf.}}}{\text{ThB}_{\text{soln.}}}$ varied simply with $\text{Pb}_{\text{soln.}}$ calculated from the known lead concentrations, i.e., the specific surface remained constant (13, 20). Assuming this constancy to hold as well for $\text{Pb}_{\text{soln.}}$ values below that in a saturated water solution, I. M. Kolthoff and C. Rosenblum (13) studied the thorium B adsorption in increasing concentrations of sodium sulfate. In these cases the calculated $\text{Pb}_{\text{soln.}}$ values represented solubilities of lead sulfate in the corresponding sulfate-ion concentrations. Since the specific surface is known from experiments in the absence of excess lattice

ion, and the volume of solution and the weight of lead sulfate may be varied at will, then a simple measurement of the ratio $\frac{\text{ThB}_{\text{surf.}}}{\text{ThB}_{\text{soln.}}}$ permits the calculation of $\text{Pb}_{\text{soln.}}$ from the definition of specific surface. Solubilities so obtained were checked by direct analysis for lead in solutions as high as $1.5 \times 10^{-3} N$ in sodium sulfate. That the calculations are justifiable is seen from table 4.

TABLE 4
Solubility of lead sulfate in sodium sulfate solutions

SODIUM SULFATE CONCENTRATION	SOLUBILITIES (23°C.)	
	Radiometric	Analytical
<i>N</i>	<i>N</i>	<i>N</i>
0	(2.8×10^{-4})	2.8×10^{-4}
5.05×10^{-4}	1.27×10^{-4}	1.34×10^{-4}
7.50×10^{-4}	0.99×10^{-4}	1.04×10^{-4}
10.0×10^{-4}	0.81×10^{-4}	0.90×10^{-4}
25.0×10^{-4}	0.56×10^{-4}	(0.60×10^{-4})
50.0×10^{-4}	0.44×10^{-4}	
75.0×10^{-4}	0.34×10^{-4}	
100.0×10^{-4}	0.31×10^{-4}	

TABLE 5
Solubility of lead sulfate in alcohol-water mixtures

WEIGHT PER CENT OF ETHYL ALCOHOL	SOLUBILITIES (25.5°C.)	
	Mg. of PbSO_4 per liter	Molarity
(Water solution)	45.1	1.49×10^{-4}
13.51	10.1	3.33×10^{-5}
29.9	1.46	0.48×10^{-5}
49.5	0.32	0.107×10^{-5}

Solubilities of lead sulfate in several aqueous alcohol solutions have also been determined in this manner. Preliminary determinations yield the data included in table 5. No claims of great accuracy are made. Rather is the method of an orienting nature, permitting close approximations to the correct solubilities in regions which are not readily susceptible to customary analytical procedures.

The validity of the mass action law at great dilutions

The sensitivity of radiometric procedures is admirably illustrated by recent tests of the validity of the mass action law as applied to the insoluble

compound radium sulfate. O. Erbacher and B. Nikitin (5, 18), and more recently B. Nikitin and P. Tolmatscheff (19), have found that the activity product of radium sulfate remains constant in sodium sulfate and sulfuric acid concentrations as high as 0.1 *N*. Table 6 illustrates some of the findings from the latter paper.

The validity of the Nernst electromotive force equation at great dilutions

Another fundamental expression which had been tested in extreme dilutions is the so-called Nernst electromotive force equation, from which it follows that for every ten-power difference in concentration of a given ion, there is a corresponding difference in electrode potential of $2.303 \frac{RT}{nF}$ volts. Since it is extremely difficult to measure the potential of an electrode of the first order containing ion concentrations as small as those involved in the handling of radioelements (10^{-8} to 10^{-14} *N*), F. Paneth and G. von Hevesy

TABLE 6
Validity of the mass action law

COMPOSITION OF SOLUTION	$\alpha_{\text{Ra}^{++}} \times \alpha_{\text{SO}_4^{--}}$
H ₂ O.....	4.17×10^{-11}
$10^{-4}N$ Na ₂ SO ₄	4.31×10^{-11}
$10^{-3}N$ Na ₂ SO ₄	4.08×10^{-11}
$10^{-2}N$ Na ₂ SO ₄	4.45×10^{-11}
Average.....	4.25×10^{-11}

(24) resorted to approximate measurements of deposition potentials of polonium, thorium B, and radium E, which, in the absence of polarization effects, equal in magnitude their electrode potentials. However, there is an insufficient concentration of radioactive ions to carry a measurable current; therefore, instead of measuring current, they determined the quantity of radioelement depositing on a noble metal at various potentials. At a voltage corresponding to the deposition potential, there should occur an abrupt increase in the amount of radioelement deposited. Their results are illustrated in figure 1, in which are found plotted the percentage deposition of radium E from two 0.1 *N* nitric acid solutions which are 10^{-9} *N* in bismuth (radium E containing no added inactive bismuth) and 10^{-4} *N* in bismuth (containing inactive bismuth nitrate), respectively, as a function of applied potential. The voltages which produce the sudden increase in deposition of radioelement are presumably the deposition potentials. From figure 1 we see that these voltages are 0.14 and 0.24 for the 10^{-4} *N* and the 10^{-9} *N* bismuth solutions, respectively, indicating that a differ-

ence in potential of 100 millivolts should be set up between two half cells containing the above amounts of bismuth. Applying the Nernst equation to the trivalent bismuth ion at the temperature of the experiment, a difference of potential equivalent to 90 millivolts was predicted. Considering the extreme difference in concentration involved, and that this work was done before the methods of purification of many radioelements had been developed, the agreement is exceedingly gratifying.

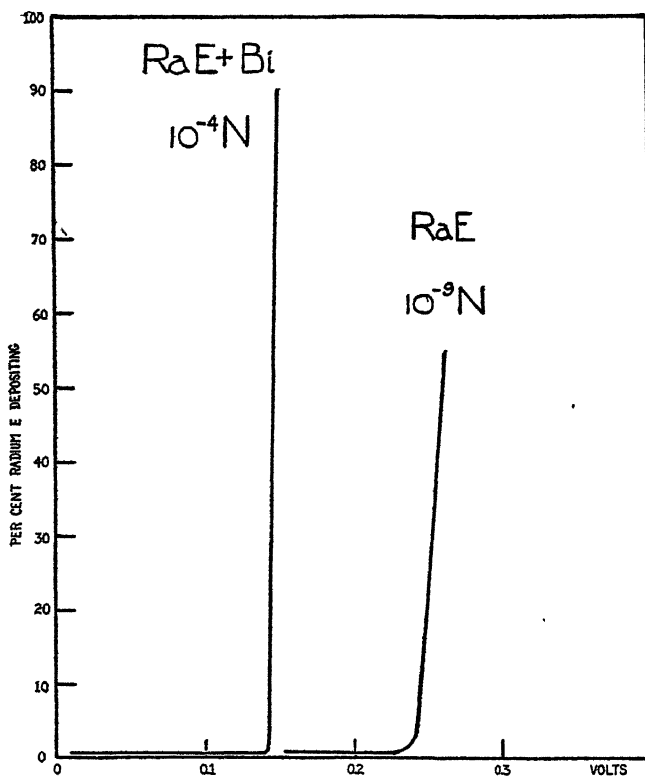


FIG. 1. Separation of radium E from 0.1 N nitric acid

An interesting application of radioactive indicators could be made in a study of the quantitative electrolytic deposition of individual metals and separation of metals. Paneth (21) emphasizes the potentialities of such electrochemical studies; and his belief seems justified by experiments (4, 32) on the mechanism of the conduction of electricity at the electrode-solution interface.

THE NATURE OF ANALYTICAL PRECIPITATES

Aged precipitates

Many studies have been made of the adsorption and coprecipitation of radioactive substances. Aside from the direct measurement of the adsorption of radioelements themselves, K. Fajans and T. Erdey-Grúz (6) have proposed a modification intended to permit the determination of the order of adsorbability of foreign ions in general. For example, when 0.4 g. of

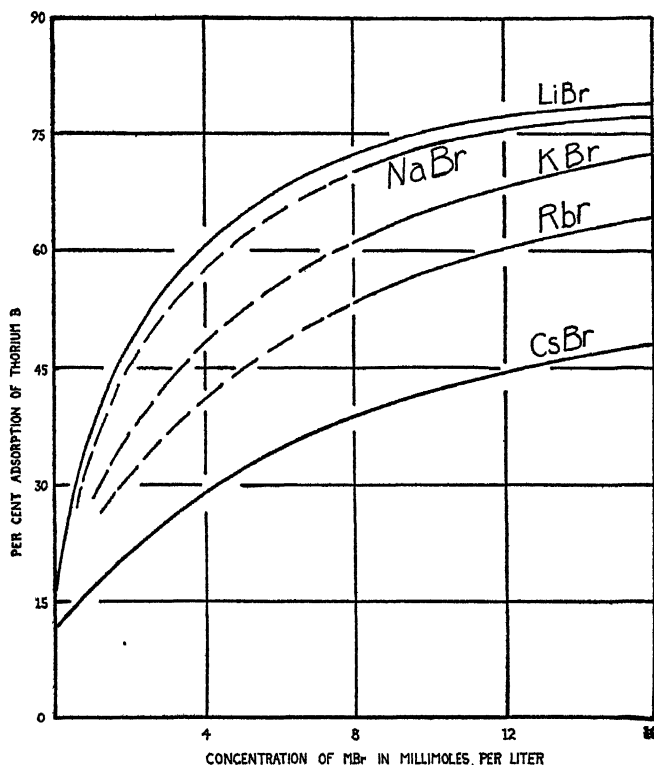


FIG. 2. Adsorption of thorium B on silver bromide in the presence of alkali bromides

silver bromide was shaken with a weakly acid solution of thorium B, only 1.8 per cent of the thorium B was adsorbed. When, however, the bromide-ion concentration was increased by the addition of potassium bromide, there occurred an increase in thorium B adsorption, until at 16 millimoles of potassium bromide per liter, 63.9 per cent of thorium B was adsorbed. Repeating these experiments with potassium chloride, an effect similar to that with bromide ion was obtained, except that the thorium B adsorption was less. Thus only 21.5 per cent of thorium B was adsorbed from a solu-

tion containing 16 millimoles of potassium chloride per liter. Fajans interprets this as indicating a smaller adsorption of chloride ion by silver bromide than of bromide ion. Adopting this procedure J. F. King and collaborators (11, 12) have determined the adsorption of various ions by thalious halides and silver bromide. Some of these findings are included in figure 2, showing the effect of alkali bromides on the thorium B adsorption by silver bromide. From the diminution in thorium B adsorption, it may be concluded that the adsorption of alkali ions is in the order $\text{Cs} > \text{Rb} > \text{K} > \text{Na} > \text{Li}$.

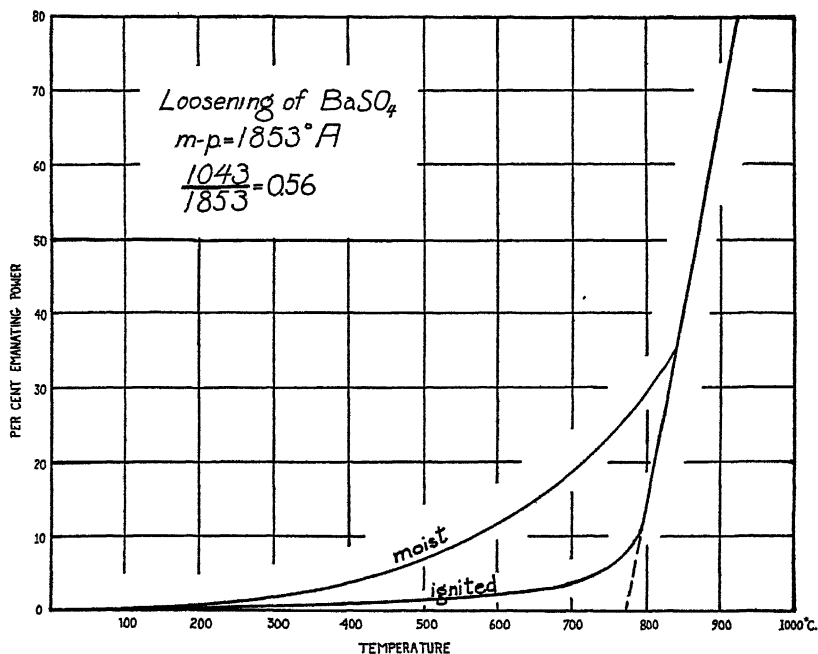


FIG. 3. Effect of heat on the emanating power of barium sulfate

O. Hahn has developed the emanation method (10) as a valuable means of investigating the mechanical properties of crystals. The procedure requires a precipitation or recrystallization in the presence of a radioelement which precedes the gaseous emanation in one of the radioactive families. Emanators most frequently used in the past have been radium and radiothorium. The quantity measured is the amount of emanation which succeeds in escaping from the crystals, expressed as per cent of the total emanation formed from the emanator. By this method, the aging of metal oxide gels has been intensively studied under various conditions

(1, 7, 8, 9). Quite illuminating is the effect of temperature on certain barium salts impregnated with a trace of radium. The effect of heat on the emanating power of barium sulfate taken from experiments of F. Strassmann (29) is shown in figure 3. The behavior of two similarly prepared samples of barium sulfate is represented. One sample was heated to 600–700°C. for three hours after precipitation, whereas the second was simply air-dried and therefore retained a considerable quantity of occluded water. Evidently the initial emanating power of the ignited precipitate is negligible and remains practically unaffected by heat until a temperature of 780°C. is attained. At this point there occurs an abrupt increase in emanating power, indicating a loosening of the crystal lattice which permits the escape of radon. The air-dried precipitate behaves somewhat differently, showing from the very beginning a gradual increase in emanating power with rise in temperature, owing to a slow distillation of occluded water which sweeps with it appreciable quantities of radon. However here, too, there is evident a sudden liberation of emanation at about 800°C., indicating that barium sulfate possesses a characteristic relaxation temperature. From present indication it would appear that such a relaxation temperature may be characteristic of many crystal powders, and occurs at an absolute temperature equal approximately to 0.5–0.6 of the absolute melting point of the substance (29).

Fresh precipitates

Considerable progress has likewise been made in understanding the nature of fresh precipitates and the processes occurring on aging at room temperature. Recent experiments (14) with the adsorption of thorium B by lead sulfate precipitates of increasing age have indicated that the fresh crystals, though apparently well formed when viewed under the microscope, are in reality spongy masses of exceedingly minute amicronic particles. These conclusions were drawn from the fact that the specific surfaces (20, 25) calculated from thorium B adsorptions were extremely large for fresh lead sulfate. Our latest experiments (15) show that fresh lead sulfate is permeable by lead ions; and even a fifty minute old sample permits a free mobility of lead ions throughout the crystal mass. This was demonstrated by adding 0.1 *N* sodium sulfate solution to a slight excess of 0.1 *N* lead nitrate solution. After a noted time (age of precipitate), thorium B was added and the whole shaken for a given time before measuring the adsorption of the radioelement. It was found that for fresh precipitates and sufficiently long shaking periods the ratio $\frac{\text{ThB}_{\text{surf.}}}{\text{ThB}_{\text{soln.}}}$ equalled the ratio $\frac{\text{Pb}_{\text{ppt.}}}{\text{Pb}_{\text{soln.}}}$. Clearly the precipitate has allowed thorium B ions, and

therefore lead ions, to diffuse freely throughout the crystals from which it is composed. A number of such experiments are graphically represented in figure 4. Here the term $Pb_{\text{exchanged}}$ is used in preference to $Pb_{\text{surf.}}$, since lead ions from crystal layers other than the outermost are involved. In the figure the $Pb_{\text{exchanged}}$ is expressed as per cent of the maximum. Repeating these experiments using radioactive lead sulfate samples yields similar curves, showing the exchange to be a reversible process. From these data it is clear that the drastic aging process occurs within the microscopic crystal, and evidently involves a growth of the primary amicronic particles.

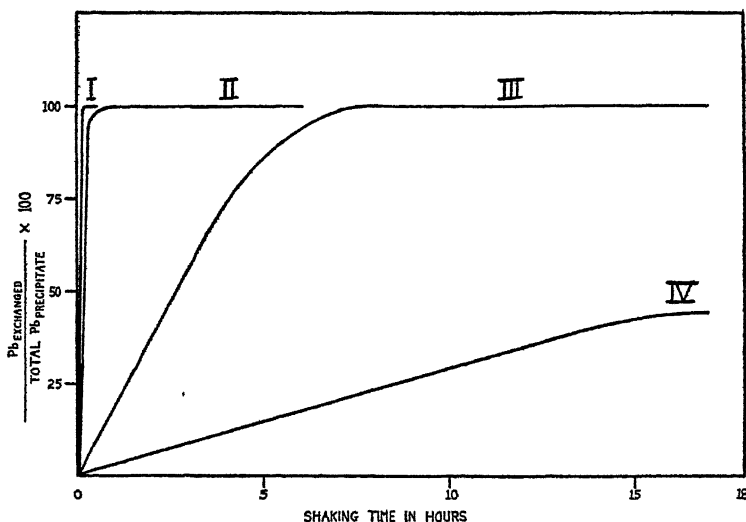


FIG. 4. Aging of lead sulfate at room temperature. I, precipitate 50 seconds old; II, precipitate 8.5-9 minutes old; III, precipitate 50-51 minutes old; IV, precipitate 3 hours old.

SUMMARY

1. Applications of radioactive indicators to microanalysis were summarized.
2. Solubility determinations made with the aid of radioelements were described.
3. The sensitivity of the methods of measuring radioactive substances permitted the examination of fundamental laws concerning the separation of ions in extreme dilutions.
4. It was found possible to study the relative adsorbability of various ions by their effect on the adsorption of thorium B.
5. The emanation method was shown to be a convenient means of studying properties of analytical precipitates.

6. The mechanism of aging processes in fresh precipitates may be studied with the help of radioelements. The example of lead sulfate aging was briefly considered.

REFERENCES

- (1) BILTZ, M.: *Z. physik. Chem.* **126**, 356 (1927).
- (2) EHRENBURG, R.: *Physikalische Methoden der analytischen Chemie*, Part I, p. 333. Bottger, Leipzig (1933). Review of previous work; literature references.
- (3) EHRENBURG, R.: *Biochem. Z.* **183**, 63 (1927).
- (4) ERBACHER, O.: *Z. physik. Chem.* **156A**, 135, 142 (1931); **163A**, 196, 215, 231 (1933); *Z. Elektrochem.* **38**, 532 (1933).
- (5) ERBACHER, O., AND NIKITIN, B.: *Z. physik. Chem.* **158A**, 216 (1932).
- (6) FAJANS, K., AND ERDEY-GRÚZ, T.: *Z. physik. Chem.* **158A**, 97 (1931).
- (7) GRAUE, G.: *Kolloidchem. Beihefte* **32**, 403 (1931).
- (8) HAHN, O.: *Ann.* **440**, 121 (1924).
- (9) HAHN, O., AND BILTZ, M.: *Z. physik. Chem.* **126**, 323 (1927).
- (10) HAHN, O., AND MULLER, O.: *Z. Elektrochem.* **29**, 189 (1923).
- (11) KING, J. F., AND GREENE, U. T.: *J. Phys. Chem.* **37**, 1047 (1933).
- (12) KING, J. F., AND PINE, P. R.: *J. Phys. Chem.* **37**, 851 (1933).
- (13) KOLTHOFF, I. M., AND ROSENBLUM, C.: *J. Am. Chem. Soc.* **55**, 2656 (1933).
- (14) KOLTHOFF, I. M., AND ROSENBLUM, C.: *J. Am. Chem. Soc.* **56**, 1264 (1934).
- (15) KOLTHOFF, I. M., AND ROSENBLUM, C.: *J. Am. Chem. Soc.* **56**, 1658 (1934).
- (16) LIND, S. C.: *J. Ind. Eng. Chem.* **7**, 406 (1915).
- (17) MAKOWER, W., AND GEIGER, H.: *Practical Measurements in Radioactivity*. Longmans, Green and Co., London (1912).
- (18) NIKITIN, B., AND ERBACHER, O.: *Z. physik. Chem.* **158A**, 231 (1932).
- (19) NIKITIN, B., AND TOLMATSCHIEFF, P.: *Z. physik. Chem.* **167A**, 260 (1934).
- (20) PANETH, F.: *Z. Elektrochem.* **28**, 113 (1922).
- (21) PANETH, F.: *Radioelements as Indicators*, p. 54. McGraw-Hill Book Co., New York (1928).
- (22) PANETH, F., AND BOTHE, W.: *Handbuch der Arbeitsmethoden in der anorganischen Chemie*, Vol. II, p. 1027. de Gruyter, Berlin (1925).
- (23) PANETH, F., AND VON HEVESY, G.: *Z. anorg. Chem.* **82**, 323 (1913); *Wien. Ber.* **122** (2a), 1001 (1913).
- (24) PANETH, F., AND VON HEVESY, G.: *Wien. Ber.* **122** (2a), 1037 (1913); *Physik. Z.* **15**, 797 (1914); *Monatsh.* **36**, 75 (1915).
- (25) PANETH, F., AND VORWERK, W.: *Z. physik. Chem.* **101**, 445 (1922).
- (26) POLESSITSKY, A.: *Z. physik. Chem.* **167A**, 394 (1934).
- (27) Report of the International Radium Standards Commission: *Rev. Modern Phys.* **3**, 427 (1931).
- (28) RUTHERFORD, SIR E., CHADWICK, J., AND ELLIS, C. D.: *Radiations from Radioactive Substances*. The Macmillan Co., New York (1930).
- (29) STRASSMANN, F.: *Naturwissenschaften* **19**, 502 (1931).
- (30) Symposium on Radioactivity: *Z. Elektrochem.* **38**, 476 (1932).
- (31) VON GROSSE, A.: *Phys. Rev.* **42**, 565 (1932).
- (32) VON HEVESY, G.: *Physik. Z.* **16**, 52 (1915).
- (33) VON HEVESY, G.: *Fortschr. Mineral. Krist. Petro.* **16**, 147 (1932).
- (34) VON HEVESY, G., AND HOBBIE, R.: *Z. anal. Chem.* **88**, 1 (1932).
- (35) VON HEVESY, G., AND RÓNA, E.: *Z. physik. Chem.* **89**, 294 (1915).

THE IMPROVED SYNTHESIS OF *o*-PHENANTHROLINE

G. FREDERICK SMITH AND C. A. GETZ

Department of Chemistry, University of Illinois, Urbana, Illinois

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INTRODUCTION

The development of the use of *o*-phenanthroline-ferrous complex as a nearly ideal, high potential, oxidation-reduction indicator by Walden, Hammett, and Chapman (6) constitutes one of the most outstanding advances of recent years in the field of analytical chemistry. Its application to many new procedures of volumetric analysis immediately followed, and former methods requiring determination by use of the potentiometric end point have been revised to include visual end point determination. The original study of the preparation of *o*-phenanthroline was made by Blau (1). The disclosure of its general and specific properties adapting it to the numerous analytical applications made its final adoption rather remarkable with regard to the time interval involved of approximately thirty-five years. As a nearly ideal example of oxidation-reduction indicator, "ferroin" (*o*-phenanthroline-ferrous ion) has its principal imperfection in the difficulty with which it is synthesized by following published descriptions of the process. The present paper has for its object the description of improvements in the preparation of *o*-phenanthroline monohydrate.

FACTORS INFLUENCING THE DEMAND FOR IMPROVED METHODS OF PREPARATION

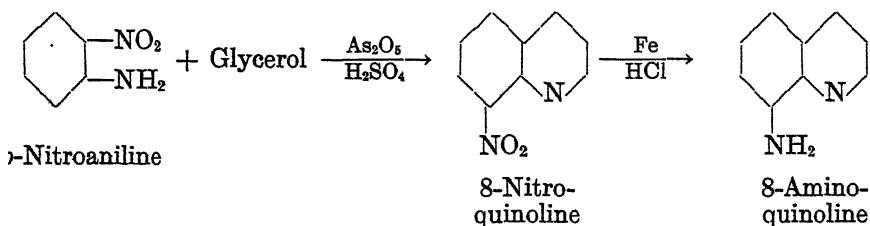
Aside from the increasing demand for the use of *o*-phenanthroline in the preparation of ferroin to be used as an indicator in volumetric determinations using such high potential oxidants as ceric sulfate, potassium permanganate, or potassium dichromate, some demand has resulted from its use as a bacteriological stain. Its use as an adsorption indicator by the process of the formation of a lake should be of possible application. It has been shown by Walden and coworkers (5) that the preparation of the nitro derivative of *o*-phenanthroline produces a product forming a ferrous complex similar to that of ferroin but having a higher oxidation potential. It would be predicted that the reduction of this nitro derivative would produce a dye base capable of the formation of a ferrous complex having a

lower oxidation potential than ferroin. Provided this amino-*o*-phenanthroline ferrous complex was not materially decreased in acid stability in the presence of oxidizing and reducing agents, its use might be desirable in titrations in the ranges of oxidation potential somewhat lower than that of ferroin. New methods for the synthesis of alkylated quinoline bases have been recently described by Darzens and Mayer (3). Following this process mono- and di-substituted *o*-phenanthroline derivatives may be synthesized. In all these cases the general principles of the improved synthesis of *o*-phenanthroline may well apply. The study of the substituted *o*-phenanthrolines of the alkylated group might be predicted to result in new types having properties more suited to their application as indicated. Unlike the nitro and amino derivatives, the oxidized forms of their ferrous complexes would be predicted to be more stable in acid solution.

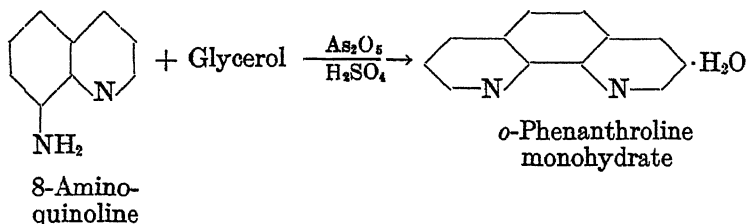
OUTLINE OF THE SYNTHESIS OF *o*-PHENANTHROLINE FROM *o*-NITROANILINE

The general scheme is outlined as follows:

First Skraup synthesis:



Second Skraup synthesis:



The first Skraup synthesis

The directions given are essentially those of Knuppel (4). A convenient amount of *o*-nitroaniline to use in this case is 2 pounds of the technical

product. A 5-liter round-bottom Pyrex flask, with one additional neck supplied, is fitted with a mercury-sealed all-metal stirring device and pulley, conveniently made by using a ball-bearing bicycle wheel hub as support. The stirrer shaft is allowed to extend for 3–4 in. through the rubber stopper closing the large opening of the flask, and a stirrer made of glass tubing is slipped over the lower portion of the drive shaft to which it is made fast, using a section of heavy-walled rubber tubing to make the attachment and protect the contents of the flask from action with metal. The design of the stirrer should be such that at 200–300 R.P.M. the contents of the flask are kept at a condition of turbulent rotary agitation. The flask is supported above an adjustable electric hot plate to provide adequate temperature control. A reflux condenser and thermometer are then attached to the second neck of the reaction flask.

Two pounds of crude *o*-nitroaniline and 2 pounds and 1 ounce of arsenic pentoxide are introduced into the flask; 4 pounds and 6.5 ounces of anhydrous glycerol are added. While stirring, 4 pounds of concentrated sulfuric acid is added gradually through the reflux condenser, in such a manner that the temperature of the reacting mixture does not exceed 110°C. After 1 hour of continuous stirring and gradual elevation of the temperature to 120°C., the stirring and elevating of the temperature is continued at the rate of 5°C. per hour until the temperature reaches 135°C. Care should be used in raising the temperature to 140°C. to prevent the reaction advancing too rapidly. Finally after 6 hours heating the reflux condenser begins to return appreciable quantities of reactants to the flask, and the amount of reflux gradually diminishes during the last 2 hours heating, as the temperature of the reaction gradually falls even while a fixed amount of heat is being applied. Finally after seven to eight hours the refluxing liquid is colorless and the reaction is complete.

The cold contents of the reaction flask are poured into a 20-gallon, acid-resisting, glazed earthenware crock to which has been added 30–40 pounds of finely chopped ice. The mixture is stirred by the use of an efficient, enameled metal, inverted, Y-shaped stirrer or substitute, saddled to the top of the earthenware container and driven by motor to provide turbulent stirring. Three and one-half pounds of caustic soda dissolved in 3 gallons of water are now added through a small-bore siphon delivery tube during a period of approximately two hours. The reaction mixture should at all times be chilled to 0°C. or lower, and additional chipped ice added as necessary. After the solution has been neutralized as tested, using litmus paper, and a slight excess of alkali has been added, the crude 8-nitroquinoline in the form of a yellowish brown precipitate is filtered, using a 14-in. Buchner funnel. The crude product precipitated from a solution of such dilution (approximately 20 gallons) requires little or no washing to be

obtained substantially free from sodium salts. The final product need not be dried before reduction to 8-aminoquinoline in the next step, and since it need not be further purified, the yield in the first two steps together is to be considered subsequently.

Reduction of 8-nitroquinoline forming 8-aminoquinoline

The directions for this reduction are followed essentially as described by Claus and Setzer (2). For working up moderately large batches of material a 12-quart, cake-mixing machine of the Hobart type is used, having a rotating and planetary motion batter-beating type of stirrer. Twelve pounds of powdered iron is mixed with just enough water to moisten the mix thoroughly, and 2.5 pounds of commercial hydrochloric acid added. To the hot mixture thus obtained the moist 8-nitroquinoline is added in small portions to maintain approximately the same temperature, adding water from time to time to replace that lost by evaporation. The iron and acid added are sufficient for the reduction of the 8-nitroquinoline from two of the first Skraup syntheses. After all the nitro compound has been added, while keeping the reaction mixture in the form of a thick paste, the reaction vessel is heated and stirred for an additional 2 hours. Finally sufficient flake caustic soda is added with stirring to neutralize the 8-aminoquinoline hydrochloride and to form sufficient iron precipitate to thicken materially the pasty reaction mixture. The aminoquinoline is then extracted, using several portions of benzene totalling 10–15 liters, and using the same mixing machine with intermediate filtration of the insoluble matter by reduced pressure in a 14-in. Buchner funnel. The benzene solution is finally concentrated by distillation at atmospheric pressure in a 5-liter, vacuum distilling, Claisen-type still until the boiling temperature reaches 100°C. Finally the 8-aminoquinoline is distilled under 25 mm. pressure, at which it boils at 175°C. A capillary air vent is used in the usual fashion to prevent bumping and to regulate pressure. The yield for the two steps thus described is approximately 50 per cent of theoretical, based upon the *o*-nitroaniline.

The second Skraup synthesis to form o-phenanthroline

Essentially the same directions and apparatus are used in the second Skraup synthesis as in the first. The reaction is much more sensitive and the heat relationships must be more closely guarded and a longer time interval should be allowed.

Two pounds of ground 8-aminoquinoline and 2 pounds of arsenic pentoxide are placed in the reaction vessel, followed by the addition of 4 pounds and 6.2 ounces of dry glycerol. Five pounds and 5½ ounces of concentrated sulfuric acid are now added in small portions through the

reflux condenser to the well-stirred glycerol and other substances. The sulfuric acid should not be added at a rate greater than that required to keep the temperature below 100°C., approximately 30 minutes being required. The mixture after the addition of all the sulfuric acid can be gradually heated to 110°C. during 1 hour, and then in 5-degree intervals per hour until a temperature of 135°C. is reached. Finally the temperature is allowed to rise to 140°C., but no higher, and maintained at this point during 2 hours. The temperature control in the case of the second Skraup synthesis should be more carefully and uniformly regulated than in the first for best results.

The cooled Skraup mixture is neutralized as described above, using, however, 40 gallons of solution as final neutralization volume rather than 20 gallons as before. Four and one-third pounds of caustic soda dissolved in 12 gallons of water should be used as neutralizing reagent. Stronger alkali for neutralization is not advised. At a time just preceding the neutralization of the entire batch a green crystalline precipitate of side reaction product forms. As the neutralization proceeds to completion, this green precipitate coagulates to form a more or less rubber-like tar. The extent to which *o*-phenanthroline is occluded by this tar is a function of the dilution of the solution in which it is formed and of the concentration of the neutralizing alkali added.

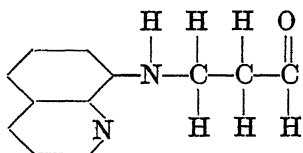
The most important controlling factors improving the yield of *o*-phenanthroline in the process described consist in the recovery of the product occluded by the tar and the preparation of water-soluble *o*-phenanthroline from the sodium salts in the neutralized Skraup mixture. Treatment of the tar as described in the literature involves drying and extraction for a long time in a Soxhlet extractor with benzene as solvent. This process, together with the formation, under unfavorable conditions, of the tar, which occludes excessive amounts of the desired product, is very tedious and inefficient. The published procedure for the separation of *o*-phenanthroline from the solution with large amounts of sodium salts involves evaporation of the solution to practically complete separation of the total solids, followed by the extraction of the desired product from the salt mass, using ethyl alcohol. This process involves the formation of considerable quantities of oily impurities and is in general unsatisfactory. Methods by which these two major difficulties can be avoided will now be described.

The separation of o-phenanthroline from the tar

The tar formed is soluble in sulfuric acid. Such a solution is prepared and diluted to 6-8 gallons with water, and the acid is then neutralized using dilute sodium hydroxide and a solution temperature of 10°C. The precipitated green crystalline product thus obtained just before the solu-

tion is neutralized now contains but little *o*-phenanthroline and by this process, repeated if necessary, a comparatively pure product can be obtained. The filtered solution of sodium sulfate and *o*-phenanthroline of approximately 10 gallons volume, if one reprecipitation is applied, is added to the main portion of 40 gallons for subsequent recovery of the indicator base.

The green precipitate was thought to be an intermediate product in the ring closure reaction of the Skraup synthesis and the following formula was postulated.



8-Aminoquinolylpropionaldehyde

The product was found to test as an aldehyde, using Schiff's reagent, and a molecular weight determination, as well as its analysis for nitrogen, carbon, and hydrogen, agree quite satisfactorily to support the assumption. The more complete identification of this compound will depend upon its purification through the formation of the picrate or perchlorate, reconversion to the parent substance, and ultimate analysis.

The product is interesting because of its reactions, which closely approach those of *o*-phenanthroline in some respects. It forms a highly insoluble perchlorate. It is a reversible oxidation-reduction indicator, giving a deep red color with oxidizing agents in mineral acid solution and a light yellow with reducing agents. Unfortunately the dye is not stable in the presence of excess of these agents, although the acid stability of the dye base is very satisfactory.

The separation of o-phenanthroline from sodium salts

Data are not at present available for the solubility of *o*-phenanthroline monohydrate in water and solutions of sodium sulfate and arsenate at different temperatures. It was originally thought possible to separate the *o*-phenanthroline from the diluted sulfuric acid solution of the second Skraup reaction products by the addition of ferrous perchlorate or ferrous sulfate, and perchloric acid in sufficient quantity to form the ferrous perchlorate complex. The product thus formed from pure *o*-phenanthroline can then be oxidized, the ferric iron thus formed removed by precipitation, and the dye base then formed by concentration of the resulting filtrate. This process was not found to be effective, for the reason that the principal impurities are precipitated as the simple perchloric acid salts at the same

time. It might well be possible to make the separation of the impurities of the nature previously described by the simple addition of perchloric acid to the dilute acid solution of the Skraup mixture, but the separation of *o*-phenanthroline from soluble sodium salts would still remain to be accomplished. It was accordingly decided to purify the tar from the neutralized reaction products as previously described, and to take advantage of the high temperature coefficient of the increase in solubility of hydrated *o*-phenanthroline in boiling aqueous solutions of the sodium salts also present, as compared with the solubility at ordinary temperatures, for the isolation of the desired product.

The 50 gallons of dilute solution of *o*-phenanthroline, sodium sulfate, and sodium arsenate is evaporated by stages in a 20-gallon, steam-jacketed, enameled, evaporating pan until the boiling solution, upon local cooling through the application of a stream of cold air, shows a cloud of minute crystals giving a milky appearance to the cooled portion of the solution. This occurs when the solution has evaporated to a volume of between 5 and 10 gallons. The reaction mixture is then allowed to cool slowly to room temperature overnight. A large portion of the crystalline *o*-phenanthroline monohydrate, together with some dark oil, is obtained. The insoluble portion containing the oily impurity is then filtered off, the concentration of the filtrate again carried out as before, and a second and third crop thus obtained. The last filtrate is finally concentrated to the point of crystallization of the inorganic salt content, which is accumulated from batch to batch until it becomes worth while to attempt to remove the last small portion of *o*-phenanthroline by extraction with hot ethyl alcohol.

The crude *o*-phenanthroline plus oily impurity is now dissolved in fifty times its weight of boiling water and clarifying carbon added, followed by filtration while still hot. The filtrate is allowed to cool and crystallize, and a second purification carried out to produce a colorless crystal mass of the finished product. The yield thus obtained is found to be 40 per cent, based upon the 8-aminoquinoline taken. The over-all yield based upon the *o*-nitroaniline used as starting material is thus found to be 20 per cent. The best over-all yield for this synthesis previously reported has been stated to be between 7 and 8 per cent.

Suggestions for further increasing production yields

The postulated composition of the side reaction product of the second Skraup synthesis suggests the possibility of so modifying conditions as to result in an increase in yield of *o*-phenanthroline at the expense of the undesired product. The failure of the 8-aminoquinolypropionaldehyde to finish the ring closure is probably due in part to a faulty ratio of sulfuric acid to arsenic pentoxide, both of which ingredients should be altered

separately to study the effect. The last step in the ring closure is in great part a dehydration reaction. The use of a higher concentration of sulfuric acid at the end of the synthesis to increase dehydrating conditions is therefore suggested. A substitute oxidizing agent to replace arsenic pentoxide has been suggested by Darzens and Mayer (3), namely, sodium *m*-nitrobenzenesulfonate. Catalysts for the arsenic pentoxide have been suggested; for example, a small amount of vanadic acid. These questions are being investigated.

SUMMARY

1. The synthesis of *o*-phenanthroline, starting with *o*-nitroaniline, has been studied with the object in view of increasing the over-all yield from the three-stage process. The improvements described resulted in an increase in yield from that previously reported of 7 to 8 per cent to that of 20 per cent.

2. The major improvements involve steps in the process for conversion of 8-aminoquinoline into *o*-phenanthroline. The prevention of tar formation in great part has been accomplished, and an improved method for the separation of the desired product from the tar-like impurities is described. The separation of *o*-phenanthroline from the large amount of sodium salts accumulated in the Skraup reaction has been much improved.

3. Suggestions concerning the nature of side reaction products have been made, and improved conditions for the Skraup synthesis in this particular case are suggested.

The material assistance of Professor C. S. Marvel throughout the progress of the above studies is hereby gratefully acknowledged.

REFERENCES

- (1) BLAU: *Monatsh.* **19**, 646 (1898).
- (2) CLAUS AND SETZER: *J. prakt. Chem.* [2] **53**, 400 (1896).
- (3) DARZENS AND MAYER: *Compt. rend.* **16**, 1428 (1934).
- (4) KNUFFEL: *Ber.* **29**, 705 (1896).
- (5) WALDEN AND COWORKERS: *J. Am. Chem. Soc.* **56**, 1092 (1934).
- (6) WALDEN, HAMMETT, AND CHAPMAN: *J. Am. Chem. Soc.* **53**, 3908 (1931).

ANOMALOUS VALENCE AND PERIODICITY WITHIN THE RARE EARTH GROUP

D. W. PEARCE

*Department of Chemistry, University of Illinois, Danville Junior College,
Danville, Illinois*

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INTRODUCTION

Overemphasis of the fact that the rare earths are uniformly trivalent has been largely responsible for the somewhat slow development of new methods for the separation of these elements. It is indeed remarkable that, until recently, almost all separations have been carried out under conditions such that all these elements were in the trivalent state. Consequently the compounds showed such slight differences in chemical and physical behavior that a large investment of time and labor was necessary in order to attain even slight success in their separation.

Recent developments in this field have shown that, while the elements may be trivalent under most conditions, variable valence is the rule rather than the exception. The application of such variations has not yet been fully worked out in many cases. It is to be expected, however, that when such applications are perfected the rare earth separations will offer only slightly more, and in some cases even less, difficulty than the separation of certain other rare elements one from the other.

A thorough survey of the literature seems to show that some investigators had early believed that valences other than three were shown by most of the rare earths. Until recently, however, such ideas were far from popular among chemists active in the work with this group of elements. It is certain that many of the early investigations were carried out unknowingly on somewhat impure materials, and this may be in some measure responsible for many of the more startling results. Unfortunately this tendency to work with impure materials, mainly through ignorance, is still with us; the literature bears frequent testimony to numerous cases in which this has been done. Results obtained by working with such materials must be applied to pure compounds with much care and circumspection.

Recently, however, certain earths have been found to possess very well developed "anomalous" valences. A stimulus, supplied by such important discoveries, appears to have been given to the work of prediction, verifica-

tion, and application of other such variable valences among the members of the group.

It is firmly believed by the writer that the application of these "anomalous" valences will, in time, bring about a revolution in the standard rare earth separation methods and will, by reducing labor and increasing efficiency, make easily available reasonable amounts of pure compounds of each of these interesting elements.

HISTORICAL

1. *Lanthanum*

In 1886 Cleve (23, 24) obtained, by means of hydrogen peroxide oxidation of lanthanum hydroxide in ammoniacal solution, an oxide which when analyzed after previous drying, showed a composition very close to La_4O_9 . The same product, when damp, apparently had the formula La_2O_5 . To Cleve it was not clear whether the increase in weight was in reality due to an oxidation or merely to the presence of hydrogen peroxide of crystallization. Melikoff and Pissarjewski (72) obtained $\text{La}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ by hydrogen peroxide oxidation in an alkaline solution in a similar manner.

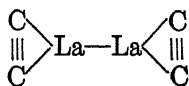
The high temperature ignition of the sesquioxide in air brought about a distinct increase (7.4–12.03 per cent) in weight, which led Kolthoff and Elmquist (59) to calculate the formulas La_2O_5 and La_2O_7 for the higher oxides. The work was repeated by Jantsch and Wiesenberger (50), however, who obtained at most a 0.5 per cent change in weight on heating La_2O_3 in air to very high temperatures. Ephraim (29) and Zschiesche (127) expressed the belief that lanthanum oxide does not absorb oxygen unless cerium is present. Marc (67) and Meyer and Koss (78) also commented on the catalytic effect of cerium on the absorption of oxygen by lanthanum oxides. On the other hand, early work by Cleve (22)—probably with impure materials—tended to show that La_2O_3 absorbed oxygen at red heat.

Higher sulfides have been prepared by Biltz (5), and by Klemm, Meisel, and von Vogel (55). The first investigator prepared LaS_2 by heating the sulfate in a stream of hydrogen sulfide. At temperatures above 600°C . the compound breaks down, giving La_2S_3 and S. It yields hydrogen persulfide with acids and apparently has the structure $\text{La}_2\text{S}_3 \cdot \text{S}$ and is a "poly-sulfide." These results would seem to be confirmed by the magnetic susceptibility measurements of Klemm, Meisel, and von Vogel, whose data show that no increase in valence occurred during the reaction.

The work of Andrieux (1) has shown the existence of borides of lanthanum and other earths having the well-defined formulas MB_6 . These were prepared by the electrolysis of fused borate and fluoride mixtures in graphite crucibles. These compounds, like the various aluminides, stan-

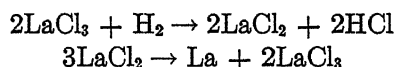
nides, thallides, plumbides, cuprides, etc., of Rossi and others (7, 31, 32, 53, 81, 95, 112), of such formulas as LaAl_4 , PrSn_3 , LaTl_3 , LaPb_3 , CeCu_2 , etc., are, in all likelihood, compounds into which enter the peculiarities of the "metallic bond." Such compounds will not be considered here.

Moissan (79), Petterson (87), and Damiens (26) have prepared the carbide LaC_2 , resembling MgC_2 . Damiens, however, was of the opinion that the compound had the structure



and that the metal was here tri- or tetra-valent and not divalent.

Some evidences of a valence lower than three for lanthanum have appeared. One is that of the hydrides prepared by Winkler (118), by Zhukov (126), and by Sieverts and Gotta (101). In these cases hydrides have been prepared which on analysis consistently give a ratio less than 3:1 for H:La. Sieverts and Müller-Goldegg (102) believed, however, that the volumes of hydrogen absorbed by the cerium group metals vary quite widely and depend on temperature and pressure conditions. Another line of evidence is that recently presented by Jantsch, Skalla, and Grubitsch (47). These investigators treated anhydrous lanthanum chloride with hydrogen at high temperatures. The following reactions apparently occurred:



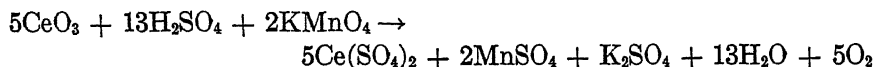
The metallic lanthanum then alloyed with the gold dish in which the reaction took place. If indeed the reactions postulated by these investigators actually represent what has taken place, then the possession of a valence of two by this element must be recognized.

2. Cerium

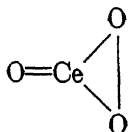
Both trivalent and tetravalent cerium compounds were known early in the history of the rare earths, the higher valence compounds being particularly characteristic. Cerium was until recently assigned to a position in Group IV of the Periodic System. In this position it presented certain anomalies, and on the discovery of hafnium was definitely relegated to its more natural position among the Group III elements.

In addition to the valences of three and four, it has often been suggested that a valence of six was shown by cerium when highly oxidized in alkaline solution. De Boisbaudran (27) confirmed the opinion of Cleve (23), who had announced the formation of "perceric hydroxide" on oxidizing $\text{Ce}(\text{OH})_3$ with hydrogen peroxide in ammoniacal solution. This compound both investigators believed to be a derivative of CeO_3 . Von Knorre (114),

Job (51), Mengel (74), Pissarjewski (88), and Meloche (72) have studied similar compounds. Mengel has used such compounds, obtained by the use of sodium peroxide as a precipitating agent, for the separation of cerium from lanthanum and didymium. Meloche prepared "perceric carbonates" and investigated in particular the method of combination of the oxygen and its availability in both acid and basic solutions. Much of the available oxygen was shown to be of the peroxide type. Schwarze and Geise (97) reported a dark red precipitate, analyzed as $\text{CeO}_3 \cdot 2\text{H}_2\text{O}$, formed by the action of ammonium hydroxide and hydrogen peroxide on cerium nitrate. This compound reduced permanganate according to the reaction:



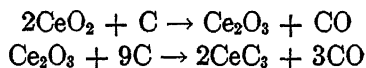
They regarded the compound, however, as a peroxide having the structure



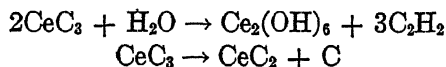
and not as a representative of hexavalent cerium. Lejeune (62) proved that the change was from Ce(III) to Ce(IV) only, but believed that Ce(VI) could exist.

Wyruboff and Verneuil (122) have reported a white oxide, Ce_3O_4 .

The unusual compound CeC_3 , prepared by reduction of the oxide with sugar charcoal at a high temperature in an electric furnace was described by Damiens (25) as a red powder. Similar work had been carried out by Sterba (108) and had resulted in the formation of an oxycarbide (or a mixture of carbide and oxide) of the formula $\text{Ce}_3\text{O}_4\text{C}_2$. Damiens believed that the red crystals contained both CeC_3 and Ce_2O_3 and that they resulted from the following reactions:



The compound reacted when treated with water or when more strongly heated:



Sterba's compound reacted less readily with water. The carbide CeC_2 has been described by Hirsch (34) and by Moissan (79).

Borides similar to those described under lanthanum have been reported by Andrieux (1).

Biltz (4) subjected ceric sulfate to the action of hydrogen sulfide at elevated temperatures. The sulfide Ce_2S_4 resulted. It reacts with hydrochloric acid to give hydrogen disulfide, and decomposes at 720°C . to give the sesquisulfide and sulfur. It would appear from these results that the compound is a polysulfide. The same compound, prepared by Klemm, Meisel, and von Vogel (55), yielded magnetic susceptibility results which would tend to show it to be a polysulfide and not a true disulfide.

On dissolving the highly oxidized hydrated oxide of cerium in concentrated hydrochloric acid an intense red color is obtained. According to James and Grant (41) this solution contains CeCl_4 , stable in concentrated acid. Koppel (60) had also prepared this compound and had studied its double salts.

The colors reported for CeO_2 and its reduction products have brought about a great deal of discussion in the literature. Sterba (107, 108) studied these oxides in some detail. His work has shown that CeO_2 is of a pale yellow color, the shade varying somewhat according to the method of preparation. On reduction of the oxide by various means certain interesting color changes resulted. By hydrogen reduction at 600°C . an indigo-blue, non-pyrophoric material—stable when completely dry but readily oxidized in moist air—was obtained. Reduction at higher temperatures gave a black, pyrophoric material, believed to contain some finely divided metal. By means of zinc reduction Sterba obtained a bluish mixture, but cadmium apparently will not reduce the ceric oxide. Meyer (40) obtained results somewhat different than those of Sterba by getting an olive-green intermediate reduction product which, on further treatment with hydrogen, became black and pyrophoric. On glowing in air the black material yielded a yellow mass of CeO_2 . Similar results were reported by Bunsen (17). Rammelsburg (93) obtained a loss of 4.7 per cent on igniting CeO_2 in hydrogen. Winkler in a similar manner obtained an oxide $\text{Ce}_2\text{O}_3 \cdot 4\text{CeO}_2$, a pyrophoric compound (119); similar substances have been reported by Brauner (9). Chase (20), by decomposing the oxalate at 550°C . in atmospheres of pure hydrogen or nitrogen, obtained a bluish-black residue which he believed was a mixture of Ce_2O_3 , Ce_2O_4 , and C. When hydrogen was used the compound was pyrophoric. Burger (18), by reduction of ceric oxide with calcium, obtained an olive-green residue probably similar to the blue and green mixtures obtained by the other investigators. Sterba and Meyer believed that their colored oxide was to be represented by the formula Ce_4O_7 . Apparently it is a mixture of Ce_2O_3 and CeO_2 .

Brauner (12) outlined the controversy over the color of CeO_2 . He believed the oxide was of a pale chamois color if pure, in which opinion Neish

concurrent (83). Spencer, however, has prepared CeO_2 which is white if ignited at low temperature and yellowish if strongly ignited (103). It was believed by Wyrouboff and Verneuil (121) that polymers of CeO_2 were responsible for the differences in color obtainable by various treatments of the same sample. They have reported para-oxides, meta-oxides, and other polymorphic forms.

It would appear from the investigations considered that: (1) CeO_2 when pure is of a pale chamois color, but the color may vary somewhat owing to methods of precipitation and temperature of ignition. (2) Reduction of CeO_2 results in the formation of certain darker colored oxides or mixtures of oxides. (3) Pyrophoric compounds may be formed by the most drastic reduction. The formation of some finely divided metal is a possibility in these cases. (4) Compounds in which cerium is hexavalent may exist.

3. *Praseodymium*

Much discussion in the literature has centered around the higher oxides of praseodymium. As early as 1865 it was noticed by Herman (33) that a "super-oxide" could be prepared, and that it yielded chlorine when treated with hydrochloric acid. The oxide Di_4O_9 or Di_2O_5 was reported by Cleve (23, 24) as having been prepared by hydrogen peroxide oxidation of "didymium" hydroxide in ammoniacal solution.

When praseodymium oxalate or the sesquioxide is ignited in air a mixture of oxides is obtained. Some higher oxide is present. The formula of this product has been the subject of much controversy. Schottlander (96), Meyer and Koss (76, 78) (by reduction and reoxidation data), and more recently Brinton and Pagel (15) and Prandtl and Huttner (91) have shown that Pr_6O_{11} is the ignition product over a wide temperature range. The last investigators believe that the constitution of the oxide is to be represented by the formula $2\text{Pr}_2\text{O}_3 \cdot \text{Pr}_2\text{O}_5$ and consider it to be a praseodymium praseodymate. Jantsch and Wiesenberger (50), while concurring with the formula, believe the substance to be merely a mixture of Pr_2O_3 and PrO_2 .

Brauner has conducted extensive research upon the oxides of praseodymium (10). From specific gravity and molecular volume considerations he has deduced the formula of the compound to be Pr_4O_7 or Pr_5O_9 . He prefers the latter formula and believes it to be the product formed when Pr_2O_3 and Pr_2O_4 react with the latter acting as an acidic oxide. By ignition of the nitrate or by fusion of the oxide with alkali nitrates, however, he obtained an oxide of jet-black color which he believed was Pr_2O_4 . His recent work substantiates his earlier claims (11). By fusing $\text{Pr}(\text{NO}_3)_3$ with sodium and potassium nitrate he was able to prepare Pr_2O_4 and, by leaching the melt with water, to separate every trace of lanthanum from

the praseodymium. Auer (2) has obtained the formula Pr_4O_7 for the ignition product of the oxalate when heated in the air.

The belief that the product may vary considerably in oxygen content, as is generally held at the present time, was put forward early in the discussion by von Scheele (115). There seems to be some evidence also that oxygen may be lost by drastic heat treatment, only to be regained on cooling.

The almost black dioxide has been prepared in a practically pure condition by Brinton and Pagel (16).

A compound Pr_2S_4 has been prepared by Biltz (5, 6) by passing hydrogen sulfide at high temperatures over the anhydrous sulfate. Higher temperatures bring about the formation of the sesquisulfide by loss of sulfur. Previously, Howe (37) commented on the oxysulfide, PrO_2S , prepared by this means. Howe believed that $\text{Pr}_2\text{S}_3 \cdot \text{S}$ resulted only in the presence of cerium, which acted as an inductor; he has suggested this as a very delicate test for the presence of cerium in praseodymium compounds. Levy (63) reports that the oxysulfide has the formula PrSO_3 .

Moissan (79) has prepared PrC_2 similar to the analogous compounds of lanthanum and cerium.

No compounds in which praseodymium has a valence lower than three would seem to have been prepared. Matignon and Cazes (70) were unable to reduce PrCl_3 by heating in an atmosphere of hydrogen at 1000°C . However, Spencer (104) has called attention to the fact that the hydride, prepared by heating the metal in hydrogen, contains insufficient hydrogen to correspond to the formula PrH_3 .

4. Neodymium

In the presence of cerium as an activator, neodymium oxide and oxalate on strong ignition in the air appear to be oxidized to higher-valenced compounds. Such results have been put forward by Meyer and Koss (78), and by Marc (67). These investigators have claimed that NdO_2 or Nd_2O_4 is formed under these conditions. Brauner has commented on the oxide Nd_2O_5 as well as Nd_2O_4 , and apparently believes that neodymium also can show a valence of six (10, 11). More recently (13) he has proved the formula Nd_2O_4 by heating the oxide in hydrogen and collecting the water obtained. The weight of the oxide Nd_2O_3 obtained and the weight of the oxygen calculated from the weight of the water gave the ratio $\text{Nd}_2\text{O}_3 : \text{O} = 1 : 1$. He prefers the doubled formula Nd_2O_4 rather than NdO_2 for the oxide.

Waegner (116) ignited the oxalate in oxygen and reported the formation of Nd_4O_7 which decomposed, on heating to higher temperatures, into Nd_2O_3 . His results have lately been disputed by Garnier and coworkers (30, 52)

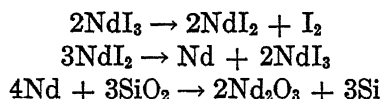
who, by means of reflection spectra, have shown the compound formed to be $2\text{Nd}_2\text{O}_3 \cdot 2\text{H}_2\text{O}$ and not Nd_4O_7 ; Hitchcock (35), during a rare earth study, obtained color changes of neodymium oxides which he interpreted to show the formation of Nd_4O_7 .

The carbide, NdC_2 , has been prepared by Moissan (80) and by Matignon (68). According to the former it is not reducible by hydrogen at red heat, reacts with chlorine to give anhydrous chlorides, and is, in general, very similar to the corresponding compounds of the other rare earths.

Several investigators have prepared and worked with the hydride. Muthmann and Beck (81) and Matignon (68, 69) obtained results showing less than three atoms of hydrogen per metal atom.

Matignon and Cazes (70) believed that the chloride should be reducible to a dichloride in a stream of hydrogen. They were unable to bring about this reaction, however, even at a temperature of 1000°C .

Jantsch, Skalla, and Grubitsch (47) have reported some evidence in favor of a valence lower than three for neodymium. The triiodide was first dehydrated and then treated with hydrogen at high temperatures. By continued heating in a silica boat some silicon was obtained. The following reactions have been proposed:



By using a gold container, neodymium-gold alloys were obtained, very clearly suggesting that the above reactions actually represent what has taken place and that neodymium can, under certain conditions, be divalent.

5. *Samarium*

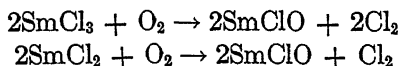
The work of Cleve (24) has shown the possibility of samarium compounds in which the metal shows a valence higher than three. The compounds apparently indicated were Sm_2O_5 and Sm_4O_9 . During a study of samarium compounds Cleve endeavored to oxidize Sm_2O_3 by heat treatment alone (23); in this, however, he was unsuccessful.

The carbide SmC_2 has been prepared by Moissan (79).

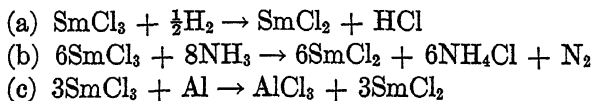
While the higher valence compounds of the element are, mainly, of doubtful nature and unimportant, the samarous compounds are well defined and of extreme importance, practically and theoretically.

Matignon and Cazes (70, 71) discovered that samaric chloride could be reduced by means of hydrogen, ammonia, or aluminum to samarous chloride. Using a Jena glass apparatus they found that reduction (with hydrogen) started at a temperature below the melting point, when the chloride became dark colored. The dichloride is of a deep red-brown

hue. It is always somewhat contaminated with oxychloride owing to the reactions:

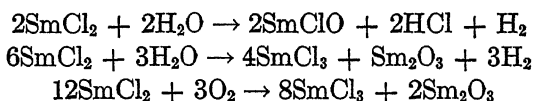


The dichloride resulted apparently from reactions such as the following:

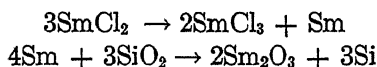


Reaction b is slower than a but, owing to the fact that it is not reversible, is preferable; reaction c must be carried out in an atmosphere of hydrogen.

The samarous chloride is insoluble and does not react with benzene, toluene, chloroform, pyridine, or absolute alcohol. In air it undergoes the following reactions:



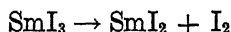
In a similar way Prandtl and Kogl (92) prepared samarous chloride and samarous bromide; the latter has a color darker than that of the chloride. When porcelain dishes were used to contain the samaric chloride being reduced (by hydrogen or ammonia), reduction of the silica took place and silicon resulted. Similarly when platinum dishes were used the higher temperatures used by these investigators caused metallic samarium to be formed, and alloys with the platinum resulted. The phenomenon is probably to be explained by the reactions:



Jantsch, Ruping, and Kunze (45) obtained samaric chloride by passing chlorine with sulfur monochloride over the heated oxide. After dehydration with hydrogen chloride it was reduced to samarous chloride by heating in a stream of hydrogen and ammonia. The dark color obtained when even traces of samarium were present suggests this as a method to show the presence of small amounts of this element in other rare earths. The dichloride so obtained was soluble in water but extremely unstable, even in an atmosphere of hydrogen. Its decomposition (as formerly commented on) was rapid in the presence of acid. The investigators showed the dichloride to be insoluble in liquid ammonia, sulfur dioxide, and hydrogen cyanide as well as in stannic chloride, phosphorus trichloride, phosphoryl chloride, and sulfuryl chloride. It was insoluble in alcohols,

ketones, amines, and esters, but slightly soluble in molten lithium or sodium chloride.

Jantsch and Skalla (46) prepared samarous iodide by the thermal decomposition of samaric iodide in a high vacuum:



The diiodide gives a deep Bordeaux-red solution more stable than that of the dichloride; it slowly decomposes, however, yielding hydrogen and a colorless solution. By double decomposition reactions Jantsch and Skalla were able to prepare samarous chromate, phosphate, and sulfate, all of which are only slightly soluble. Samarous sulfate is a bright orange-yellow salt, soluble with decomposition in dilute acids. The diiodide decomposed on heating according to the following reaction, which commenced at 560°C:

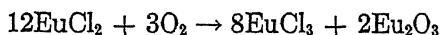


The writer has been unable to reduce samarium trichloride in dilute sulfuric acid solution by the electrolytic method using a mercury cathode and high current densities.

Klemm and Rockstroh (56) obtained the molecular volumes and melting points of the dichloride and iodide and compared them with their data for the similar properties of the trihalides. The melting points of the dihalides are, as would be expected, the higher in each case.

6. *Europium*

In 1911 Bourion and Urbain discovered (8) the new compound europous chloride, EuCl_2 . This was prepared by the reduction of europic chloride by hydrogen. The white amorphous material dissolved in water without noise or residue and gave a fairly stable solution. In the hot, however, the following reaction occurred:



These investigators also attempted to reduce EuOCl with hydrogen at red heat. They obtained, however, only an insignificant loss of weight; EuO apparently cannot be prepared in this way.

Jantsch, Alber, and Grubitsch (42) prepared europous chloride and europous iodide, and have shown that the triiodides are easier to reduce than the trichlorides. Europous iodide is a brownish green, almost black, in color; its solutions, however, are colorless and quite stable, giving only a slight evolution of hydrogen. The solution is a great deal more stable than the solution of the corresponding samarium compound. Europic iodide has so great a tendency to decompose that these investigators

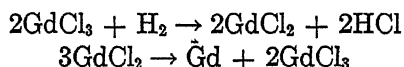
found it impossible to prepare it in the anhydrous condition by means of the action of hydrogen iodide and hydrogen on the hydrated salt. However, it was found that the best method for the preparation of europous iodide from europic iodide was to heat a mixture of the latter hydrated salt and ammonium iodide in a stream of the gases mentioned above.

Yntema (124) discovered the fact that europic chloride might be reduced electrolytically to europous chloride at the surface of a mercury cathode. In the presence of sulfate ion europous sulfate was precipitated. The colorless salt was fairly stable and could be filtered out, thus enabling an excellent separation of europium to be made from other rare earths which remained in solution.

W. E. Pearce (84) was able to reduce europic chloride in dilute sulfuric acid solution using a platinum, rather than a mercury, cathode. Attempts to prepare europous chromate by electrolytic reduction of europic chromate were unsuccessful. He was able, however, to reduce the higher chloride by means of magnesium, aluminum, and iron; in each case the powdered metal was merely slowly sifted into a solution of the chloride in water to which a small amount of sulfuric acid had been added. In attempts to obtain reduction with stannous chloride, ferrous sulfate, hydrazine sulfate, hydroxylamine sulfate, and hypophosphorous acid negative results were obtained.

7. *Gadolinium*

No compounds of gadolinium in which the metal shows an anomalous valence have been prepared. However, the work of Jantsch, Skalla, and Grubitsch (47) has shown that the following reactions may be brought about under sufficiently drastic treatment:



The gadolinium metal so formed then alloyed with the gold dish in which the reaction took place. These reactions, supported as they are by parallel cases in which elements known to show divalence react in an exactly similar way, show clearly that under some conditions gadolinium may have at least a transitory valence of two.

8. *Terbium*

Urbain and Jantsch (111) have investigated the higher oxides of terbium. According to these investigators low temperature ignition yields the dark brown to black oxide Tb_4O_7 , while temperatures greater than 1600°C . break down this compound with the loss of oxygen. Urbain had earlier (110) obtained the dark brown oxide on ignition of the oxalate, and

a black oxide when the sulfate was decomposed. James and Bissel (40) prepared a black oxide, apparently Tb_4O_7 , by ignition of the oxalate. Levy (64) believes that in this case, because of the remarkable persistence of the color given to a mixture of oxides by only a trace of terbium, salt formation is very probable. No experimental evidence, however, has been offered in support of this view.

Potratz (89) reported a carbide, TbC_3 . This was obtained when the formate or acetate was ignited in a closed crucible. No analyses of the product were reported.

7. *Dysprosium*

Urbain and Jantsch (111) were unable to oxidize Dy_2O_3 by strongly heating in oxygen, nor were they able to reduce it by heating in an atmosphere of hydrogen to very high temperatures. Klemm and Schuth (58) were unable to reduce dysprosium trichloride with hydrogen at high temperatures.

Jantsch, Jawurek, Skalla, and Gawalowski (43) have investigated the halides of the terbium and erbium groups. They were able to obtain no lower-valence compounds of dysprosium, but did obtain small amounts of the metal by heating the triiodide in a high vacuum in the proximity of fresh barium metal similarly heated. The results were interpreted to mean merely that the vapor of the triiodide had reacted with the barium, and not that any lower-valence compound had been obtained.

8. *Holmium*

The great rarity and difficulty of separation of holmium has prevented any very thorough investigation of its compounds; no valences other than that of three have been suggested for this element.

9. *Erbium*

Cleve (23, 24) believed that erbium formed the oxide Er_2O_5 in addition to the normal sesquioxide Er_2O_3 . He had also previously announced (23) his preparation of the oxide Er_4O_9 . It is extremely likely that his materials were quite impure. No recent investigator has confirmed this discovery. Klemm and Schuth (58) were unable to reduce the trichloride, and Jantsch and coworkers (43) have obtained no evidence of an anomalous valence for this element.

10. *Thulium*

Jantsch, Skalla, and Grubitsch (48), while working with the halides of thulium and lutecium, could isolate no divalent compounds resulting from high temperature treatment of the trihalides with hydrogen. Metallo-

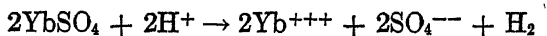
graphic and analytical examination of the gold dishes used in the experiments indicated, however, that some dihalide had been present, since its decomposition was the only tenable explanation for the presence of thulium-gold alloy within the dish. That the gold itself had no influence on the formation of the rare earth metal was clearly proved by the fact that the same reaction took place when porcelain boats were used, except that, in these cases, some silicon dioxide was reduced by the metal. A further evidence for the formation of some thulous chloride was believed to be the dark color of the higher salt after treatment for a certain length of time in the hydrogen stream. The investigators believe that thulous chloride, like divalent samarium compounds, is very dark in color. The existence of more than a very small amount of thulous chloride was, however, not shown by the analyses. The fused salt after cooling gave only a slight evolution of hydrogen when treated with water. They were also unable to prepare thulous iodide, although all indications seemed to show that the reactions had been similar.

While thulous sulfate would be expected to be insoluble like samarous sulfate, it would appear from experimental work by the author that Tm^{+++} is extremely difficult to reduce electrolytically in aqueous solution.

11. Ytterbium

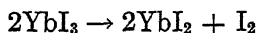
In 1929 Klemm and Schuth (58) announced the preparation of ytterbium dichloride, by the reduction of anhydrous ytterbium trichloride with hydrogen. The material was heated for six hours at 600–620°C. and for half an hour at 850–900°C. in the hydrogen stream. The dichloride obtained was light grey, almost white; the water solution, however, was yellowish green.

Ball and Yntema (3) extended the method of the latter for the separation of europium (124) and were able to precipitate YbSO_4 from aqueous solution by reducing Yb^{+++} to Yb^{++} in dilute sulfuric acid solution. The same method has been used by Prandtl (90) to prepare pure ytterbium, and by the author (85) for the thorough separation of ytterbium from thulium and from lutecium fractions. These investigators have all commented on the reaction of the yellowish green YbSO_4 with the dilute acid as soon as the current is cut off:

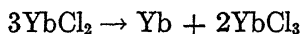


The author and coworkers (86) have shown that the form of the YbSO_4 precipitate may be varied from fine crystalline needles to coarse spheres by means of controlled reduction conditions. The latter form is highly advantageous for use in the separation of ytterbium, as its reaction with dilute acid is negligible.

Jantsch, Skalla, and Jawurek (49) have shown that ytterbium triiodide if heated in vacuum above 500°C. reacts quickly according to the equation:



The diiodide is black by reflected light but by transmitted light is red in the central portions of the mass and almost colorless through the edges. At 250°C. ytterbium triiodide commences to split off halogen strongly; the reaction begins for the bromide at 700°C. and for the chloride at 870°C. The same investigators have prepared the dichloride; they found, however, that it was best prepared by hydrogen reduction. The dichloride dissolved in water to give the yellow-green solution and slowly evolved hydrogen. The reaction



prevented the determination of the melting point of this compound. The dibromide is described as being of a golden yellow color.

12. *Lutecium*

Jantsch, Skalla, and Grubitsch (48) obtained the same reactions for lutecium halides as for the corresponding thulium compounds. That is, all the evidence pointed toward the intermediate formation of a dichloride which, when heated strongly, decomposed to form the metal and the tri-chloride. Lutecium dichloride is, however, probably white.

Klemm and Schuth (58) have commented on the effect of lutecium dichloride as an impurity on their results obtained when measuring the magnetic susceptibility of ytterbous chloride.

The recent work of Jantsch and Klemm (44) has not ascribed a definite valence of two to any of the elements lanthanum, gadolinium, or lutecium; this is, in all probability, due to the fact that while evidence points to the intermediate formation of lower-valence compounds, these have not yet been obtained in such a state as to permit their analyses and a study of their properties.

PERIODICITY IN VALENCE

It was probably R. J. Meyer who first pointed out that a periodicity in properties existed among the members of the rare earth group (77). He believed in the uniform trivalency and great similarity of lanthanum, gadolinium, and lutecium and placed them together in Group III of the Periodic Table; the remaining earths were distributed among groups following the third. More recently Brauner and Svagr have attacked the problem of the relative basicities of the rare earths (14). They considered the influence of the hydrolysis of the sulfates on the inversion of sucrose

and on the hydrolysis of methyl acetate. Gadolinium was found, by this method, to have a basicity close to that of lanthanum. Brauner has therefore placed the former element under lanthanum in his arrangement of the rare earths in the Periodic Table in order to bring out this relation. Both Meyer and Brauner believe that the rare earth group is well placed when the members are spread out across the Table. Such an arrangement certainly throws most of these elements into unnatural groupings with the common elements, and suggests relations in their chemical properties which do not appear to exist. Both investigators seem to ignore the fact that the periodicity shown by their measurements is *among the rare earths themselves*. This periodicity does not necessitate that a close relation exist between the members of the rare earth group on the one hand and the remaining elements in the system on the other, and should not then be used as a justification for the spreading out of the group which, in the opinion of the author, confuses rather than clarifies the basis for such grouping.

Recently published work by Sherwood and Hopkins (99), who also sum-

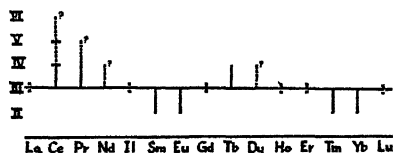


FIG. 1. Anomalous valence within the rare earth group

marized previous measurements on the relative basicity of the rare earths, does not show this relation between gadolinium and lanthanum. Their results, however, agree in general with those previously obtained by other investigators. It would appear that the measurements of Meyer and of Brauner are complicated by the entrance of other unknown factors.

Von Hevesy (113) presented a schematic diagram which exhibited the tetravalent tendencies of cerium, praseodymium, and terbium as well as the fact that samarium and europium could show divalence. The later discovery by Klemm and Schuth (58) of the divalence of ytterbium allowed this element to be added to the diagram (54, 57). As filled out by Klemm, the diagram also shows a possible tetravalence for dysprosium and divalence for thulium. In figure 1 is shown such a schematic diagram. Here certain valences are questioned; their existence must be regarded as still not conclusively proved. If the series shown in the figure is examined it can be seen that, with respect particularly to valence, "*every eighth element resembles the first.*" Thus we have the following groupings.

1. *Lanthanum, gadolinium, and lutecium*

None of these three shows any permanent, well developed valence other than the normal one of three. From the point of view of the electronic structure of the atom lanthanum, No. 57 (2, 8, 18, 18, 8, 3), would certainly be expected to be trivalent only. There is no tendency for an electron of the kernel to leave a completed shell and become a valence electron. Gadolinium, No. 64 (2, 8, 18, 18 + 7, 8, 3), apparently possess a comparatively stable structure, and lutecium, No. 71 (2, 8, 18, 18 + 14, 8, 3), marks the close of the fourth quantum group with its full quota of 32 electrons. Lutecium also, owing to its completed kernel, would be expected to show no tendency toward a valence other than two. If, however, the results of Jantsch and coworkers be construed to show a transitory divalence for lanthanum, gadolinium, and lutecium, the resemblances still stand, in whatever manner the existence of these extra valences be explained electronically.

The discussion by Clark (21) also brings out the similarity between these three elements, showing, as it does, the close relation of their normal spectral terms.

2. *Cerium and terbium*

Sidgwick (100) has reasoned that cerium, No. 58 (2, 8, 18, 18 + 1, 8, 3), shows its additional valence of four, owing to its possession in the fourth quantum group of an extra electron which may be rather easily removed. When the loss of this electron takes place a reversion to the stable inner structure of lanthanum is brought about. Thus also, it might be reasoned, does terbium, No. 65 (2, 8, 18, 18 + 8, 8, 3), show tetravalence by a reversion to the gadolinium kernel. But the extra valence in this case is not as well-marked as that of cerium, owing to the fact that the tendency to revert to the gadolinium structure is not as strong as that of cerium to revert to the structure of lanthanum. The carbides CeC_3 and TbC_3 , previously described, heighten the similarity between these two elements, whatever type of valence is present in these compounds.

3. *Praseodymium and dysprosium*

Praseodymium, No. 59 (2, 8, 18, 18 + 2, 8, 3), which has two extra electrons over the number possessed by lanthanum, can lose one of these and show tetravalence. Here, however, the only tetravalent compound so far obtained is the oxide; this fact may be taken to show the lesser stability of praseodymic than ceric compounds. It would, of course, be expected on the above reasoning that praseodymium should show a valence of five. The compounds of Brauner and others may represent this tendency. In the case of dysprosium, related to praseodymium as ter-

bium is to cerium, a valence of four is expected. Urbain and Jantsch (111) were unable to obtain even the oxide Dy_2O_4 . The oxide Dy_2O_5 was announced by Cleve, but criticism of the material and other interpretations of the results might be offered.

4. *Neodymium and holmium*

These two elements, as far as can be stated at the present time, show no similarities in valence relationships. Brauner and others firmly believe in the tetravalence of neodymium under some conditions, but insufficient work has been done with pure holmium compounds to allow of any comparison. No evidence we have points to any valence other than three for the latter element.

5. *Illinium and erbium*

The great rarity of illinium has so far precluded any detailed study of its properties. In the case of erbium it would appear that no anomalous valences are shown.

6. *Samarium and thulium*

Samarium, No. 62 (2, 8, 18, 18 + 5, 8, 3), can show a valence of two, and apparently thulium, No. 69 (2, 8, 18, 18 + 12, 8, 3), can also under some conditions. Hughes and the author (38) have expressed as their opinion, based on magnetic susceptibility measurements, that the extra electron, left behind when divalence is shown in cases such as this of samarium, is in some manner repressed and is associated more closely with the 4_f orbital group. This might be construed as a tendency for the samarium kernel to become as nearly as possible like that of gadolinium. Very similar conclusions on this point have recently been published by Selwood, who clearly expresses his ideas in a valuable contribution (98). He refers to this tendency as "a striving to reach the normal condition of lanthanum, gadolinium, or lutecium" desirable "because these three elements alone are in S states, they have no multiplet structure, the orbital component of magnetic moment in each is lacking." Of course this reasoning again appears somewhat at a loss, since it would apparently call for thulium, No. 69 (2, 8, 18, 18 + 12, 8, 3), to show a greater tendency toward divalence than does samarium, because lutecium has a more stable electronic configuration than that of gadolinium. But work to date would certainly show that samarium has a "stronger" valence of two than has thulium. It must be admitted, however, that existent methods of determining the "strength of the tendency" to show these anomalous valences are far from good. They depend merely upon the apparent ease with which the anomalous compound is obtained and upon its stability. The periodicity in

basicity shown by the results of Brauner and of Meyer is probably in some way connected with these phenomena. Electrochemical measurements conducted on such elements in anomalous valence states should supply invaluable data for the clarification of these difficulties.

7. Europium and ytterbium

Europium, No. 63 (2, 8, 18, 18 + 6, 8, 3), is very readily reduced to divalence. The tendency to retain the gadolinium kernel is strong. In a similar way ytterbium, No. 70 (2, 8, 18, 18 + 13, 8, 3), is easily reduced, and the dry ytterbous salts are fairly stable. The extra electron, not being used in valence forces, apparently becomes associated with the others in

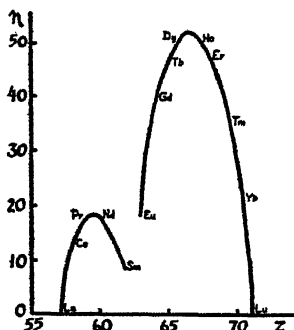


FIG. 2. Magnetic susceptibilities of the rare earths

the fourth quantum group, increasing it in effect to the completed number of 32.

MAGNETISM AND VALENCE

The great paramagnetism of the rare earth metals and their compounds is one of their outstanding properties. The use of the magnetic balance, in addition to providing a means of identification and a test of purity for these elements, has thrown considerable light on their electronic structure and the changes undergone by the various atoms on reduction and oxidation. It has enabled several problems to be solved, partially at least, which would by any other means be exceedingly difficult to attack.

Zernike and James (125) summarized previous measurements of the paramagnetism of the rare earths and compared them with their own results. These values are, in general, in good concordance with those calculated by Hund (39) on the assumption that the number of electrons in the $4f$ orbital group varies from zero in the case of lanthanum to fourteen for lutecium.

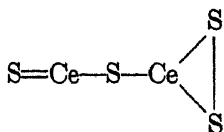
In figure 2 is shown the discontinuous curve obtained by plotting the magnetic susceptibility against the atomic number (109).

The results of St. Meyer (106) and of Cabrera (19) show that the sus-

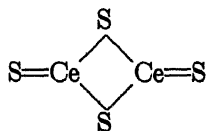
ceptibility values of ceric and praseodymic compounds fall in close proximity to those of the corresponding lanthanum and cerous compounds, respectively. In a similar way the work of Klemm and Rockstroh (56) brings out the fact that the susceptibility of a samarous compound is near that of the corresponding europic compound. Klemm and Schuth (57, 58) have determined the susceptibility of a sample of somewhat impure ytterbous chloride. They believe that the divalent ytterbium ion is diamagnetic.

Hughes and the author measured the susceptibilities of certain europous, europic, ytterbous, ytterbic, and gadolinium compounds (38). The results, when considered along with those of previous investigators, are seen to bear out the law that *the susceptibility of a rare earth ion in a valence of four approaches that of the ion of atomic number one less in the valence of three; also the susceptibility of a rare earth ion in a valence of two approaches that of the ion of one greater atomic number in the valence of three.* The recent work of Selwood (98) adds confirmation to this view. These facts can only be interpreted to mean that on reduction for instance, the third electron—that one not in use for valence forces—is suppressed and becomes closely associated with the 4_f orbital group. Obviously it is that same inner group which is affected on oxidation and is forced to give up an electron for valence uses. We thus arrive at electronic structures for certain of the rare earth ions as shown in table 1.

The usefulness of magnetic susceptibility measurements has already been mentioned. Klemm, Meisel, and von Vogel (55) actually used this principle when they proved that the compound Ce_2S_4 was a polysulfide of trivalent cerium rather than a simple sulfide of tetravalent cerium. This was shown to be the case as the susceptibility was the same as that of Ce_2S_3 . According to the principle stated in the last paragraph, if there had been a valence change there would have been a large change in the magnetic susceptibility, since the sulfide of quadrivalent cerium should have the same susceptibility as La_2S_3 . These considerations indicate that Ce_2S_4 is a cerous compound with a possible structure



whereas if it were a ceric compound it might have a structure



COLOR AND VALENCE

Since the rare earth atoms differ, as far as orbital electrons are concerned, apparently only in the fourth quantum group, it would be expected that the colors are mainly due to the degree of incompleteness of this shell. Color relations, then, might be expected to be periodic just as are anomal-

TABLE 1

Electronic structures of certain rare earths in various valence states

ATOMIC NUMBER	ELECTRONS IN KERNEL	ION	K	L	M	N	O	P VALENCE ELECTRONS
57	54	La ⁺⁺⁺	}	8	18	18	8	3
58	54	Ce ⁺⁺⁺⁺						4
58	55	Ce ⁺⁺⁺	}	8	18	18 + 1	8	3
59	55	Pr ⁺⁺⁺⁺						4
59	56	Pr ⁺⁺⁺	2	8	18	18 + 2	8	3
62	59	Sm ⁺⁺⁺	2	8	18	18 + 5	8	3
62	60	Sm ⁺⁺	}	8	18	18 + 6	8	2
63	60	Eu ⁺⁺⁺						3
63	61	Eu ⁺⁺	}	8	18	18 + 7	8	2
64	61	Gd ⁺⁺⁺						3
65	61	Tb ⁺⁺⁺⁺						4
65	62	Tb ⁺⁺⁺	}	8	18	18 + 8	8	3
66	62	Dy ⁺⁺⁺⁺						4
66	63	Dy ⁺⁺⁺	2	8	18	18 + 9	8	3
69	66	Tm ⁺⁺⁺	2	8	18	18 + 12	8	3
69	67	Tm ⁺⁺	}	8	18	18 + 13	8	2
70	67	Yb ⁺⁺⁺						3
70	68	Yb ⁺⁺	}	8	18	18 + 14	8	2
71	68	Lu ⁺⁺⁺						3

ous valence relations, the latter so evidently owing to this shell and its gradual increase from 18 to 32 electrons. Lanthanum and gadolinium, cerium and terbium, praseodymium and dysprosium, etc., should be similarly colored. That this is not the case is shown by the last pair and many succeeding pairs in which the elements are first and eighth.

The origin of the colors of the rare earth ions is obscure. They have, however, generally been assumed to be due to the incompleteness of this $4f$ orbital group, where also the highly variable and large paramagnetic forces presumably arise (61, 105). Also Yntema (123) has put forward his opinion that the colors originate in this level. He was led to this conclusion by a study of the absorption bands of the various ions and their apparently regular shift toward higher frequency with increase in atomic weight.

Again, reasoning from the kernel structures as derived from magnetic susceptibility measurements, we might expect the ceric ion to be the same color, or very nearly the same color, as the lanthanum ion, praseodymic as cerous, samarous as europic, europous as gadolinium, and ytterbous as lutecium. These colors are certainly not similar in any instance. But in

TABLE 2
Colors of certain rare earth ions in normal valence states

La ⁺⁺⁺ 57	(Colorless).....(Colorless)	71 Lu ⁺⁺⁺
Ce ⁺⁺⁺ 58	(Colorless).....(Colorless)	70 Yb ⁺⁺⁺
Pr ⁺⁺⁺ 59	(Irish green).....(Apple green)	69 Tm ⁺⁺⁺
Nd ⁺⁺⁺ 60	(Red to violet).....(Rose-red)	68 Er ⁺⁺⁺
Ho ⁺⁺⁺ 61	(Probably yellow).....(Yellow)	67 Ho ⁺⁺⁺
Sm ⁺⁺⁺ 62	(Pale yellow).....(Yellow)	66 Dy ⁺⁺⁺
Eu ⁺⁺⁺ 63	(Pale pink).....(Colorless)	65 Tb ⁺⁺⁺


 Gd⁺⁺⁺ 64 (Colorless)

each case except that of europium, the element when in the anomalous valence state is more highly colored than when in the normal valence condition. In the words of G. N. Lewis (65), "we may still say that a colorless substance is converted into a colored substance by a loosening of the electronic structure." The compounds of the rare earths in anomalous valence are more unstable electronically than are the compounds of these elements in the normal valence state, and one outward expression of this instability is increased color. This view is quite in keeping with all our experimental evidence bearing on this problem.

Other facts, however, enter to complicate the question of color and its origin. These facts consist of two relationships which can be pointed out.

1. Let us compare the color, first of the extreme members of the group, then of the second with the second from the last, and so on. We arrive at the data shown in table 2.

This color sequence was discussed by Main Smith (66). He believed that the relation was due to the fact that, after deducting 54 (the number of planetary electrons in the normal xenon atom) from the number of planetary electrons in the rare earth ion, one of two similarly colored ions has as many electrons more than zero as the other has less than fourteen. Thus Nd^{+++} , for example, has 57 electrons, less 54 gives 3; for Er^{+++} , $14 - (65 - 54) = 3$. The full significance of this relation is still not apparent but, on the face of it, it means that in the N shell the number of electrons increases from $18 + 0$ in lanthanum to $18 + 14$ in lutecium, and that two subgroups of the rare earths may be considered to exist, the one from lanthanum to gadolinium inclusive, the other from gadolinium to lutecium inclusive. Gadolinium is therefore common to both subgroups. The color sequence, however, can still not be considered as explained.

2. The colors of bivalent rare earth ions show an interesting resemblance to the colors of the trivalent ions of the elements which immediately

TABLE 3
Colors of bivalent rare earth ions

ATOMIC NUMBER	ION	COLOR	COLOR	ION	ATOMIC NUMBER
61	La^{+++}	Yellow?	Orange-yellow	Sm^{++}	62
62	Sm^{+++}	Pale yellow	Colorless	Eu^{++}	63
68	Er^{+++}	Rose-red	Brick-red?	Tm^{++}	69
69	Tm^{+++}	Green	Green	Yb^{++}	70

precedes. This relationship is shown in table 3. The evidence for the brick-red color of Tm^{++} was obtained by the author in one experiment during attempts to reduce Tm^{+++} by means of high current densities on a mercury cathode. Attempts to obtain this color in other experiments by the same method were unsuccessful, but no explanation other than that mentioned above seems adequate.

VALENCE AND SEPARATIONS

It was pointed out in the introduction that rare earth separations were tedious, time-consuming, and wasteful because, in general, the methods employed were of such a type that they perforce dealt with elements which were in the same valence state and hence were chemically similar in the extreme. This difficulty of separation and purification is, without doubt, itself the chief reason why better methods have not been developed! Recently the pure compounds have become more available; materials which it has taken years to prepare offer opportunities of research which often

result in the discovery of new properties and new and better separation methods. In the case of only a very few of the fifteen elements need it now be said that their rarity is the biggest factor in the difficulty of preparing them. An examination of the "intermediate fractions" in any rare earth laboratory would reveal that it is the inefficient separation methods and not the rarity of the elements that causes the trouble in most cases.

Rolla and Fernandez (94), from a study of the solubilities of the double magnesium and double manganese nitrates of the earths of the cerium group, evolved an exceedingly ingenious separation method. The solubility of the pure double manganese and double magnesium nitrates in water increases with increasing atomic number; however, the solubility, in the solid state, of a double manganese nitrate in the corresponding double magnesium salt was found to decrease with increasing atomic number. Therefore crystallization of a mixture of these double salts of the cerium group rapidly concentrated the earths of higher atomic number in the liquor and soluble end of the series, and the earths of lower atomic number in the crystals and insoluble end. This, however, is still but a fractional method.

It was discovered quite early in the history of the group that cerium could be removed most easily from the other elements by oxidizing it to tetravalence and precipitating it in that state. Various oxidizing agents such as potassium bromate, potassium permanganate, chlorine, etc., have been used. The most efficient method, however, is probably that of electrolytic oxidation, perfected by Neckers and Kremers (82). The sulfate or nitrate solutions are electrolyzed and a soluble phosphate is added after anodic oxidation has taken place, whereupon ceric phosphate is precipitated. The rare earths may be rendered cerium-free in one operation, but the gelatinous phosphate occludes much of the mother liquor and the precipitate must be treated several times to prepare pure cerium compounds.

Electrolytic reduction methods for the separation of highly pure europous and ytterbous sulfates have already been mentioned. It would be a valuable addition to rare earth methods if samarium could be separated in a like manner. It seems probable that the use of solvents other than water might bring about the desired result.

Brauner (13) has introduced the method of fusion with potassium nitrate, often used for the removal of traces of cerium, to the separation of praseodymium and neodymium. He has claimed that, under temperature control, oxidation of the praseodymium to tetravalence takes place and that a good separation of the resulting Pr_2O_4 from the $\text{Nd}(\text{NO}_3)_3$ may be obtained by extracting the melt with water.

Willard and Fowler (117) undertook the separation of mixtures of cer-

tain rare earths by a partial thermal decomposition of the sulfates followed by leaching with water. They first determined the products formed in such decompositions and the dissociation pressures of the pure anhydrous sulfates at definite temperatures. The attempt was then made to maintain the partial pressure of the sulfur trioxide above the heated, mixed isomorphous sulfates at a value intermediate between those of the constituents and thus cause a complete decomposition to the insoluble oxide of the one compound without affecting the other, remaining as the soluble sulfate. Following these principles a separation of cerium from the other earths was obtained, owing to the fact that the cerous sulfate ignited easily to ceric oxide, while the other rare earths remained as the trivalent sulfates. A partial separation only of praseodymium from lanthanum was possible, as the sulfate of the former ignited only partially to the higher-valence oxide and as only that which was oxidized was separable. In attempting to separate rare earths which when ignited did not tend to oxidize no success was obtained, owing to the fact that the salts, being isomorphous, gave solid solutions the dissociation pressures of which were intermediate between those of the pure constituents. Thus the decomposition products themselves formed solid solutions and no great solubility differences between the constituents existed. Very similar work has recently been carried out by Wohler and Flick (120).

The separation of terbium has always been accomplished only with very great difficulty. This is due not so much to its great rarity, although it is one of the least abundant of the rare earths, but largely to its position in the group and its proximity to the abundant gadolinium on the one side and to the rare dysprosium on the other. If indeed the peculiar compound TbC_3 can be prepared, it is very likely that a better method for the separation of terbium is at hand. Thus the oxide will in all probability be extractable from the carbide, or vice versa. Certainly the method would be only fractional, and its application to the preparation of cerium by taking advantage of the compound CeC_3 would be no improvement over the present efficient methods, but there may be here at hand a welcome method for the separation of terbium.

Kalischer and the author, in unpublished work, have determined the temperatures at which certain rare earth nitrates lose some and all of their molecules of water of crystallization. When some mixtures of such carefully heated, partially dehydrated nitrates are extracted with anhydrous ether at low temperatures, separations are obtained. Some of these have been reported by Hopkins and Quill (36). It seems probable that the ease of dehydration depends in some way upon the ability of the element in question to exhibit anomalous valence, probably because there is a variation in the strength of coördination valences holding the water molecules.

It is also extremely likely that the degree of dehydration affects the solubility in ether. The full meaning of the experimental data at hand has not yet been worked out.

In the newer chemistry of the rare earths—the chemistry of the “anomalous valences”—much still remains to be done, in spite of the great contributions of Jantsch, Klemm, and others, both abroad and in this country. The study of this group is not exhausted; indeed it still presents many problems that are fresh and new, and that challenge the ingenious mind to devise methods of attack.

REFERENCES

- (1) ANDRIEUX: Chem. Abstracts **23**, 4893 (1929).
- (2) AUER: Monatsh. **6**, 477 (1885); Sitzber. Akad. Wiss. Wien **92**, II, 317 (1885).
- (3) BALL AND YNTEMA: J. Am. Chem. Soc. **52**, 4264 (1930).
- (4) BILTZ: Ber. **41**, 3341 (1908).
- (5) BILTZ: Z. anorg. Chem. **71**, 427 (1911).
- (6) BILTZ: Z. anorg. Chem. **122**, 195 (1922).
- (7) BILTZ AND MEYER: Z. anorg. Chem. **176**, 23 (1928).
- (8) BOURION AND URBAIN: Compt. rend. **153**, 1155 (1911).
- (9) BRAUNER: Monatsh. **86**, 174 (1885–86).
- (10) BRAUNER: Proc. Chem. Soc. **14**, 71 (1898); **17**, 70 (1902); Z. anorg. Chem. **32**, 1 (1902).
- (11) BRAUNER: Chem. News **77**, 161 (1898); **83**, 197 (1901).
- (12) BRAUNER: Z. anorg. Chem. **34**, 207 (1903).
- (13) BRAUNER: Collection Czechoslov. Chem. Communications **5**, 279 (1933).
- (14) BRAUNER AND SVAGR: Collection Czechoslov. Chem. Communications **4**, 49, 239 (1932).
- (15) BRINTON AND PAGEL: J. Am. Chem. Soc. **45**, 1460 (1923).
- (16) BRINTON AND PAGEL: J. Am. Chem. Soc. **51**, 42 (1929).
- (17) BUNSEN: Ann. **105**, 45 (1858); Pogg. Ann. **155**, 376 (1875).
- (18) BURGER: Ber. **40**, 1652 (1907).
- (19) CABRERA: Compt. rend. **180**, 668 (1925); J. phys. **6**, 252 (1925).
- (20) CHASE: J. Am. Chem. Soc. **39**, 1576 (1917).
- (21) CLARK: Electronic Structure and Properties of Matter, p. 63. John Wiley and Sons, New York (1934).
- (22) CLEVE: Bull. soc. chim. [2] **39**, 151 (1883).
- (23) CLEVE: Bull. soc. chim. [2] **43**, 53 (1885).
- (24) CLEVE: Chem. News **53**, 45 (1886).
- (25) DAMIENS: Compt. rend. **157**, 335 (1913).
- (26) DAMIENS: Ann. chim. phys. **9–10**, 137 (1918).
- (27) DE BOISBAUDRAN: Compt. rend. **100**, 605 (1885).
- (28) EPHRAIM: Inorganic Chemistry, English edition, p. 732. Gurney and Jackson, London (1926).
- (29) GARNIER: Arch. sci. phys. nat. **40**, VI, 93, 199 (1915).
- (30) GUILLET: Rev. mét. **19**, 352 (1922).
- (31) HANAMAN: Intern. Z. Metallog. **7**, 174 (1916).
- (32) HERMAN: J. prakt. Chem. **82**, 385 (1865).
- (33) HIRSCH: Trans. Am. Electrochem. Soc. **20**, 57 (1911).

- (35) HITCHCOCK: J. Am. Chem. Soc. **17**, 525 (1895).
(36) HOPKINS AND QUILL: Proc. Nat. Acad. Sci. **19**, 64 (1933).
(37) HOWE: J. Am. Chem. Soc. **34**, 148 (1912).
(38) HUGHES AND PEARCE: J. Am. Chem. Soc. **55**, 3277 (1933).
(39) HUND: Z. Physik **33**, 855 (1925).
(40) JAMES AND BISSEL: J. Am. Chem. Soc. **36**, 2060 (1914).
(41) JAMES AND GRANT: J. Am. Chem. Soc. **37**, 2652 (1915).
(42) JANTSCH, ALBER, AND GRUBITSCH: Monatsh. **53-54**, 305 (1929).
(43) JANTSCH, JAWUREK, SKALLA, AND GAWALOWSKI: Z. anorg. Chem. **207**, 353 (1932).
(44) JANTSCH AND KLEMM: **216**, 80 (1933).
(45) JANTSCH, RUPING, AND KUNZE: Z. anorg. Chem. **161**, 210 (1927).
(46) JANTSCH AND SKALLA: Z. anorg. Chem. **193**, 391 (1930).
(47) JANTSCH, SKALLA, AND GRUBITSCH: Z. anorg. Chem. **216**, 75 (1933).
(48) JANTSCH, SKALLA, AND GRUBITSCH: Z. anorg. Chem. **212**, 65 (1933).
(49) JANTSCH, SKALLA, AND JAWUREK: Z. anorg. Chem. **172**, 207 (1931).
(50) JANTSCH AND WIESENBERGER: Monatsh. **60**, 1 (1932).
(51) JOB: Ann. chim. phys. [7] **20**, 205 (1900).
(52) JOYE AND GARNIER: Compt. rend. **154**, 510 (1912).
(53) KETTEMBEIL: Z. anorg. Chem. **38**, 213 (1904).
(54) KLEMM: Z. anorg. Chem. **187**, 29 (1930).
(55) KLEMM, MEISEL, AND VON VOGEL: Z. anorg. Chem. **190**, 133 (1930).
(56) KLEMM AND ROCKSTROH: Z. anorg. Chem. **176**, 181 (1928).
(57) KLEMM AND SCHUTH: Z. anorg. Chem. **184**, 345 (1929).
(58) KLEMM AND SCHUTH: Z. anorg. Chem. **184**, 352 (1929).
(59) KOLTHOFF AND ELMQUIST: J. Am. Chem. Soc. **53**, 1225 (1931).
(60) KOPPEL: Z. anorg. Chem. **18**, 305 (1898).
(61) LADENBURG: Z. Elektrochem. **26**, 270 (1920).
(62) LEJEUNE: Compt. rend. **191**, 665 (1930).
(63) LEVY: The Rare Earths, 2nd edition, p. 196. Arnold, London (1924).
(64) Reference 63, p. 216.
(65) LEWIS: Valence and the Structure of Atoms and Molecules, p. 161. The Chemical Catalog Co., New York (1923).
(66) MAIN SMITH: Nature **120**, 583 (1927).
(67) MARC: Ber. **35**, 2382 (1902).
(68) MATIGNON: Compt. rend. **131**, 891 (1900).
(69) MATIGNON: Chem.-Ztg. **24**, 1062 (1900).
(70) MATIGNON AND CAZES: Ann. chim. phys. [8] **8**, 417 (1906).
(71) MATIGNON AND CAZES: Compt. rend. **142**, 83, 276 (1906).
(72) MELIKOFF AND PISSARJEWSKI: Z. anorg. Chem. **21**, 70 (1899).
(73) MELOCHE: J. Am. Chem. Soc. **37**, 2338, 2645 (1915).
(74) MENGEL: Z. anorg. Chem. **19**, 71 (1899).
(75) MEYER: Z. anorg. Chem. **37**, 378 (1903).
(76) MEYER: Z. anorg. Chem. **41**, 94, 97 (1904).
(77) MEYER: Naturwissenschaften **2**, 781 (1914).
(78) MEYER AND KOSS: Ber. **35**, 3740 (1902).
(79) MOISSAN: (a) Compt. rend. **122**, 357 (1896); (b) *ibid.* **123**, 148 (1896); (c) *ibid.* **124**, 1233 (1897); (d) *ibid.* **131**, 595, 924 (1900).
(80) MOISSAN: Compt. rend. **131**, 595 (1900).
(81) MUTHMANN AND BECK: Ann. **331**, 46 (1904).
(82) NECKERS AND KREMERS: J. Am. Chem. Soc. **50**, 955 (1928).

- (83) NEISH: J. Am. Chem. Soc. **31**, 517 (1909).
(84) PEARCE, W. E.: Master's thesis, University of Illinois, 1931.
(85) PEARCE: Thesis, University of Illinois, 1934.
(86) PEARCE, QUIRKE, AND HOPKINS: Am. J. Sci. Forthcoming publication.
(87) PETTERSON: Ber. **28**, 2419 (1895).
(88) PISSARJEWSKI: Z. anorg. Chem. **31**, 359 (1902).
(89) POTRATZ: Chem. News **92**, 3 (1905).
(90) PRANDTL: Z. anorg. Chem. **209**, 13 (1932).
(91) PRANDTL AND HUTTNER: Z. anorg. Chem. **136**, 289 (1924).
(92) PRANDTL AND KOGL: Z. anorg. Chem. **172**, 265 (1928).
(93) RAMMELSBURG: Pogg. Ann. **108**, 40 (1859).
(94) ROLLA AND FERNANDEZ: Gazz. chim. ital. **57**, 704 (1927); Atti accad. Lincei [6] **7**, 370 (1928).
(95) ROSSI: Atti accad. Lincei **17**, 182, 839 (1933).
(96) SCHOTTLANDER: Ber. **25**, 378, 569 (1892).
(97) SCHWARZE AND GEISE: Z. anorg. Chem. **176**, 209 (1928).
(98) SELWOOD: J. Am. Chem. Soc. **56**, 2392 (1934); **55**, 4869 (1933).
(99) SHERWOOD AND HOPKINS: J. Am. Chem. Soc. **55**, 3117 (1933).
(100) SIDGWICK: The Electronic Theory of Valency, p. 43. The Oxford Press, Oxford (1929).
(101) SIEVERTS AND GOTTA: Z. anorg. Chem. **172**, 1 (1928).
(102) SIEVERTS AND MÜLLER-GOLDEGG: Z. anorg. Chem. **131**, 65 (1924).
(103) SPENCER: Trans. Chem. Soc. **107**, 1265 (1915).
(104) SPENCER: The Metals of the Rare Earths, p. 109. Longmans, Green and Co., London (1919).
(105) ST. MEYER: Naturwissenschaften **8**, 284 (1920).
(106) ST. MEYER: Physik. Z. **26**, 51, 478 (1925).
(107) STERBA: Compt. rend. **133**, 221 (1901).
(108) STERBA: Ann. chim. phys. **362**, 193 (1904); Compt. rend. **134**, 1056 (1902).
(109) STONER: Magnetism and Atomic Structure, p. 167. Methuen and Co., London (1926).
(110) URBAIN: Compt. rend. **141**, 521 (1905).
(111) URBAIN AND JANTSCH: Compt. rend. **146**, 127 (1908).
(112) VOGEL: Z. anorg. Chem. **72**, 319 (1911); **75**, 41 (1912); **91**, 277 (1915).
(113) VON HEVESY: Die seltenen Erden vom Standpunkte des Atombaues, p. 31. Springer, Berlin (1927).
(114) VON KNORRE: Z. angew. Chem. **10**, 685, 717 (1897).
(115) VON SCHEEL: Z. anorg. Chem. **17**, 310 (1898); **18**, 352 (1892); Ber. **32**, 409 (1899).
(116) WAEGNER: Z. anorg. Chem. **42**, 118 (1904).
(117) WILLARD AND FOWLER: J. Am. Chem. Soc. **54**, 496 (1932).
(118) WINKLER: Ber. **23**, 2642 (1890); **24**, 873 (1891).
(119) WINKLER: Ber. **24**, 873 (1891).
(120) WOHLER AND FLICK: Ber. **67B**, 1679 (1934).
(121) WYROUBOFF AND VERNEUIL: Compt. rend. **124**, 1230 (1897); **127**, 863 (1898); **128**, 501 (1899); Bull. soc. chim. [3] **21**, 118 (1899); Ann. chim. phys. [5] **9**, 289 (1907).
(122) WYROUBOFF AND VERNEUIL: Ann. chim. phys. [9] **8**, 289 (1906).
(123) YNTEMA: J. Am. Chem. Soc. **48**, 1598 (1926).
(124) YNTEMA: J. Am. Chem. Soc. **52**, 2782 (1930).
(125) ZERNIKE AND JAMES: J. Am. Chem. Soc. **48**, 2827 (1926).
(126) ZHUKOV: Ann. inst. phys. Chem. **3**, 461 (1926); **3**, 6000 (1927).
(127) ZSCHIESCHE: J. prakt. Chem. **107**, 65 (1869).

THE EFFECT OF STRUCTURE ON THE REACTIVITY OF SOME ORGANIC HALOGEN COMPOUNDS

EDITH WILSON¹

Chicago, Illinois

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Laws that govern the reactivity of organic compounds are still unknown, although countless studies have been made on the various phases of isolated systems. On account of the important rôle of organic halogen compounds in organic synthesis there has been a never-ceasing endeavor to learn the laws governing the reactivity of this group. Up to the present time the rates of reaction can be predicted in only a few cases.

Thermodynamics has given much information on the free energy and heat of combustion of organic compounds, but for the halogen compounds the available data of this type are of doubtful reliability; however, there is every reason to anticipate that reliable data will be available in the near future. The free energy and the heat of combustion data have aided little in solving the question of the time which a reaction will require to reach equilibrium. For a solution of this question theoretical speculation is directed toward the energy of activation. There is no general law known for the calculation of the energy of activation. From temperature coefficient data values of the energy of activation are calculated, but such values are restricted to the experimental accuracy of the data. These values of the energy of activation sometimes differ from the values obtained from spectroscopic data. This disparity of values emphasizes the possibility that energy factors other than the energy of activation may be entering into the values obtained. It has not been proven that the actual energy required to break the bond is the same as the energy of activation, and so far theory has not taken this factor into account. Nor have the number of degrees of freedom among which the energy must be distributed before reaction may occur been taken out from the realm of speculation. It is not surprising, therefore, that so little has been known about the fundamental nature of the reactivities of compounds.

In the absence of any fundamental laws for predicting rates of reactions, it was hoped that a study of the isolated systems of organic halogen com-

¹ Present address: Universal Oil Products Co., 310 S. Michigan Ave., Chicago, Illinois.

pounds would yield information which might be correlated into a general scheme dealing with the effect of the structure in the reactivity of the organic halogen compounds.

THE RÔLE OF THE SOLVENT IN RATE MEASUREMENTS

Reactions with organic halogen compounds that lend themselves to reaction rate measurements usually take place in a solvent and are bimolecular in character. The rate constants are obtained by using relationships which hold for gaseous systems. That such calculations might be justified was first shown by Eyring and Daniels (29), who found that the character of the rate of the unimolecular decomposition of nitrogen pentoxide was unaffected by the presence of an inert solvent, although the actual values of the rate constants varied somewhat for different solvents. Work of Norrish and Smith (87) on the reaction of *p*-nitrobenzyl chloride and trimethylamine showed a discrepancy of about 10^8 in magnitude between the experimental values of the rate constants in solution and the values of the hypothetical rate constants for gaseous reactions obtained by employing the same critical increment as found from the experimental values. They agreed with Christiansen (15) that a deactivating effect due to the presence of the solvent, where the value of the critical increment is lowered by the solvent, would best explain this discrepancy.

In a detailed and exhaustive study Moelwyn-Hughes (76, 77) continued this work of the correlation of reaction rates in solution and in the gaseous phase. He found that reactions fell into two types: the one to which most reactions belong showed an agreement between the two values; the other showed a disagreement of about 10^8 in the two values. This work indicated that the mechanism of reaction by collision would adequately account for reaction rates in inert solvents as well as reaction rates in the gaseous phase. Either factors other than collision must play an important rôle in reaction rates in solution because of the existence of the second type of reaction, or the number of collisions must be greatly affected by the solvent. In the case of two reactions which showed a lower reaction rate in solution, namely, triethylamine with ethyl iodide and ethyl alcohol with acetic anhydride, Moelwyn-Hughes and Hinshelwood (79) found by experiment that an inert solvent, such as carbon tetrachloride or hexane, could not account for the lower value of the rate constant, since the lower value held for the gaseous reaction. These authors believed the most promising explanation of the discrepancy in the values was the effect of the ionization of the molecules.

The validity of the interpretation given by Moelwyn-Hughes and Hinshelwood has been criticized by Lewis and Hudleston (66), Polissar (97), and La Mer (61), who have pointed out that there is no theoretical justification

for the assumption that collisions in solution are of the same nature as collisions in the gaseous phase. In general, they believe a correct treatment of reaction rates in solution is probably not obtained by the simple application of the Arrhenius equation. Although the temperature range for reactions in solutions is small and the variation of the energy of activation with the temperature may be negligible for the reactions studied, it appears doubtful whether such a variation may be completely neglected as Moelwyn-Hughes and Hinshelwood have done. The fact that reactions in solution appear to have a practically constant value for the collision number may be a mere matter of fortuity, since possibly reactions of this kind occur frequently and easily lend themselves to measurements.

Although the relative magnitude of the reaction rate constants in solution may be independent of the solvent, Menshutkin (73, 75) showed as early as 1890 that the actual value of the rate constant did depend to some extent on the nature of the solvent. Menshutkin was able to list a number of organic compounds in terms of one which appeared to be the most inert solvent. This list has remained essentially unchanged. Little is known of the nature of solvents; still the work of Langmuir (59) on the orientation of molecules at the surface of a liquid and that of Stewart (126) on the x-ray studies of liquids have indicated that the fields of force about the various parts of an organic molecule may account for what is known as the solvent action of a particular compound. The most inert solvents are symmetrical compounds, such as hexane and carbon tetrachloride. In these inert solvents the values of the reaction rate constants in solution vary the least from the values of the reaction rate constants in the gaseous phase. So also the fields of force about these solvents vary the least. For solvents in which various atoms or groups of atoms are present in the molecule, the fields of force vary for the different parts of the molecule. This non-uniformity of the fields of force undoubtedly exerts different effects on the substance dissolved, depending to some extent on the nature of the solute. How much this non-uniformity in the fields of force would affect the rate of a reaction can only be roughly estimated from the place occupied by the solvent in the list of solvents. In general, at least for a number of solvents, this effect will be small in comparison to the effect produced by the structure of the compound reacting.

THE EFFECT OF STRUCTURE ON THE RATE OF REACTION

From the theoretical considerations there is not a satisfactory treatment for reaction rates in solution, but many studies have been made in which reaction rate measurements have been used to obtain information on the relative reactivity of organic compounds. It has been considered permissible to assume that trends in reaction rates of organic compounds with

similar types of structure reacting with the same substance under the same conditions are an indication of the influence exerted by the structure of the organic radical. In most organic reactions more than one reaction may occur, but usually one of the reactions proceeds at a much greater speed, making the slower one relatively unimportant. Among the various alkyl isomers the slow reaction for one isomer may become the rapid reaction for another. It is believed that if the structure of an organic radical does play a part in the rate of reaction with organic compounds, a comparison of various series would show this effect. The actual rate of the reaction will vary with different reactants and solvents. In some cases the influence exerted by either reactant or solvent may be greater than the influence exerted by the structure of the organic halide. Obviously, the complete story of reactivity must include consideration of all these factors; however, the discussion will be focused on only one phase, the effect of the structure of the organic halide. On this basis certain effects may find explanation in the story of the reactant or solvent.

The organic halogen compound is a dipole. In determining the properties of the halides, electric fields of force must play an important part. In order to use a broader concept, which would include the effects of all other fields of force, it has been considered that the strength which binds the halogen atom to a carbon atom is determined by the force of the resultant for the carbon atom holding the halogen atom and the remaining three atoms or groups of atoms attached to the carbon atom. Thus all halogen compounds are considered as methyl halides or methyl halide derivatives. It follows that the rate of reaction of different halides with the same substance will depend on the relative force holding the halogen atom to the carbon atom, and the variations in the rate must be a result of the structure of the groups attached to the carbon atom holding the halogen atom. This study of the rate constants proceeds on the assumption that the particular groups attached to the central carbon atom determine the specific rate of the compound.

It has long been accepted that, save for a few exceptions, the reaction rates of the various halogens increase in passing from the fluoride to the iodide, and it is deemed unnecessary to present here data to show this.

The effect of one alkyl radical

The methyl halides are the simplest halides and will be used as reference compounds where data permit. The simplest variation from this structure is the replacement of a hydrogen atom by an alkyl group. Many measurements have been made with alkyl halides and various substances. Results for reaction rate constants that are available for straight chain primary alkyl halides are given in table 1. The data are recorded in the

TABLE 1
Rate constants of primary alkyl halides

COMPOUND	(a) WISL- CENUS (141)	(b) WILDER- MAN (139)	(c) HECHT, CONRAD, AND BRUCKNER (43)	(d) MEN- SCHUTKIN (73)	(e) BURKE AND DOWAN (9)	(f) PRESTON AND JONES (98)	(g) PRESTON AND JONES (98)	(h) SEGALLER (101)	(i) ACREE AND SHAD- INGER (1)	(j) COX (19)	(k) COX (19)	(l) CONSTANT (16)	(m) HARTER, MEER, AND POLÁNYI (41)
	Mini- mum time in minutes	$K_{30^\circ}/$ min.	$K_{30^\circ}/$ min	$K_{100^\circ}/$ hr.	$K_{24.5^\circ}/$ min.	$K_{40^\circ}/$ min.	$K_{40^\circ}/$ min	$K_{42.5^\circ}/$ min.	$K_{25^\circ}/$ min	$K_{40^\circ}/$ min.	$K_{40^\circ}/$ min	$K_{60^\circ}/$ hr.	$T_{275^\circ\text{C.}}$
CH_3X	4.5		0.06490	Rapid	0.000935	2.5	0.4730	0.033620	7.20	0.053070	0.04725		10000
$\text{C}_2\text{H}_5\text{X}$	40.0	0.00162	0.00510	0.06080	0.002200	0.0324	0.0311	0.007003	3.16	0.014220	0.01159	0.196	7000
$\text{C}_3\text{H}_7\text{X}$	170.0	0.00052	0.00180	0.01160	0.000984	0.0076	0.0098	0.002788	0.20	0.007130	0.00536	0.104	4400
$\text{C}_4\text{H}_9\text{X}$				0.00830	0.000686			0.002544	0.2140			0.101	3300
$\text{C}_6\text{H}_{11}\text{X}$								0.001147				0.128	2200
$\text{C}_8\text{H}_{13}\text{X}$								0.002436	0.0094			0.125	
$\text{C}_9\text{H}_{15}\text{X}$			0.00110	0.0065				0.002408				0.122	
$\text{C}_{12}\text{H}_{25}\text{X}$			0.00105	0.0060				0.002389	0.0159			0.134	
$\text{C}_{14}\text{H}_{29}\text{X}$												0.102	
$\text{C}_{16}\text{H}_{33}\text{X}$												0.098	
$\text{C}_{18}\text{H}_{37}\text{X}$												0.0905	
$\text{C}_{20}\text{H}_{41}\text{X}$								0.002140	0.0013			0.0890	

(a) $\text{RI} + \text{CH}_3\text{COCHNACOOCC}_2\text{H}_5$ in alcohol.
 (b) $\text{RI} + \text{KOH}$ in alcohol.
 (c) $\text{RI} + \text{NaOCC}_2\text{H}_5$.
 (d) $\text{RI} + \text{N}(\text{C}_2\text{H}_5)_3$ in acetone.
 (e) $\text{RI} + \text{AgNO}_3$ in alcohol.
 (f) $\text{RI} + (\text{iso-C}_6\text{H}_{11})_3\text{N}$ in alcohol.
 (g) $\text{RI} + (\text{CH}_3)_2\text{NCC}_6\text{H}_5$ in alcohol.
 (h) $\text{RI} + \text{C}_6\text{H}_5\text{ONa}$ in alcohol.
 (i) $\text{RI} + \text{Na } \alpha\text{-naphthoxide}$ in alcohol.
 (j) $\text{RI} + \text{Na } \beta\text{-naphthoxide}$ in alcohol.
 (k) $\text{RI} + \text{KI}$ in acetone.
 (l) $\text{RI} + \text{Na(v)}$.

same form as found in the original sources. This was done in preference to calculating to a relative basis, because it was felt that the original form would give the more exact picture of the character of the results. In many cases sufficient temperature data to enable a calculation to a standard temperature are not available. The specific rate was found to depend on the concentration in many cases and a calculation to a standard concentration would not be permissible. The results of Haywood (42) are not included on account of their doubtful nature as pointed out by Goldsworthy (35). With the exception of the results of Wislicenus (141) and of Hartel and Polányi (40), the results in table 1 are given as rate constants. The results of Wislicenus are given as the time for the reaction to go to completion. As the first recorded work of this kind, these qualitative results are of interest in that the same trend was observed as in the later work. Hartel and Polányi (40) have shown that the diameter of a sodium vapor flame when reduced by burning in the presence of an organic halogen compound is inversely proportional to the square of the pressure of the halides and may serve as a measure of the speed of the reaction. With the diameter of the flame held constant, the partial pressure of the various halides has been determined. Using an arbitrary scale for which the pressure of methyl chloride was taken as 10,000, the other halides are expressed on a relative scale. These relative values are given in the last column of table 1. The value of methyl iodide is 1, so the lower values mean a greater speed; thus the results of Hartel, Meer, and Polányi (41) show an increase in the speed of the reaction in passing from methyl to the higher members of the series. The reaction is a gaseous one, and the value of the speed of the reaction was obtained by the use of an entirely different line of attack from that used to obtain the rates of reaction in solution.

The outstanding character of this series of results with the exception of those of Hartel, Meer, and Polányi is the decrease in the rate with the increase in the number of $-\text{CH}_2-$ groups in the alkyl radical. The amount of the decrease is the greatest between the lower members of the series and becomes less between the higher members, but the decrease does not disappear with the first four or five members, as it is evident among the highest members that have been tested. Burke and Donnan (9) found a greater rate for ethyl than methyl iodide with ethyl alcohol as the solvent. Segaller (101, 202) found that sodium ethylate and sodium phenolate reacted more rapidly with the iodides in ethyl alcohol than in methyl alcohol. There is no satisfactory explanation of these differences, but they are doubtless related to the fact that the degree of dissociation varies more for the lower members of the series and the fact that the association of the lower members is much greater than for the other members of the series. Although there are a few cases which are exceptions to the rule, it seems

justifiable to conclude that there is a real and consistent decrease in the values of the rate constants in passing from methyl to the ethyl halides. Under special conditions this decrease may be masked by other factors. The value for amyl iodide in the work of Segaller is unexpectedly low. In the early work most of the amyl iodide was obtained from grain alcohol and contained some isoamyl alcohol. Only in the more recent work, where the amyl halides were obtained synthetically, should the values for these halides be given serious consideration. The values of Acree and Shadinger (1) and those of Conant and Hussey (16) do not show a consistent decrease with an increase in the number of $-\text{CH}_2-$ groups in the alkyl group. There is a decided trend toward a decrease in both data, and it seems that some experimental errors probably crept into the values or that the initial iodides contained traces of impurities.

The effect of two or three alkyl groups

It has been shown that the replacement of one hydrogen by an alkyl radical in a methyl halide produces a decrease in the rate of the reaction of the halide. It would be expected that the replacement of a second or third hydrogen by an alkyl radical would further reduce the rate of reaction of the substituted methyl halide. In this fact alone there is nothing new, as it is merely the well-known rule in organic chemistry for secondary and tertiary compounds. In table 2 are data for the reaction rate constants of primary, secondary, tertiary, and iso halides. The results of Brusoff (8) using alkyl iodides and sodium ethylate in methyl alcohol are expressed in the time for the evolution of 20 cc. of olefin, while those of Lengfeld (64) using alkyl bromides with potassium ethylate are the per cent of change in the halide after the reaction has been allowed to proceed for one day.

Several experimenters have used the isopropyl, butyl, and amyl halides in their reactivity studies. The isopropyl halides are not strictly comparable to the isobutyl and isoamyl halides because the two latter are primary compounds. In table 2 the isopropyl halides have been placed under the secondary column rather than under the iso column. All workers found that the isoamyl halides reacted faster than the isobutyl halides. It seems that this increase could not be attributed solely to the purity of the isoamyl halide. Since only two members of the series are present in the data, it cannot be said that this increase in the rate constant with increase in length of the chain holds for the series. However, it does appear that while the presence of a branched chain causes a decrease in the reaction rate as compared to the straight chain for the first members of the series, this decrease becomes less and less as the branching is further removed from the halogen atom, so that the rate constants for the series increase somewhat in ascending the series.

There are comparatively little data for the secondary compounds, but what there are show a decrease in the rate as compared to the primary compound. Segaller's work, using alkyl iodides and sodium ethylate, showed a gradual decrease in the values with an increase in the number of $-\text{CH}_2-$ groups in the alkyl radical. Isopropyl alcohol is, in reality, a secondary compound in structure, and the chemical properties place it with the secondary rather than the iso compounds. The rates of the iso halides seem to tend to be less than those of the secondary compounds. If the isopropyl iodide acts in reality more like a secondary compound, or if it can act readily in one of two ways, the diversity in the nature of the values for isopropyl iodide would be explained. Contrary to all other work, the work of Hartel, Meer, and Polányi shows a marked increase in the rate of the secondary over the primary halides.

Perhaps less is known about the tertiary alkyl series than other substituted halides, since even reactions of the first members of the series have proven difficult to understand. The ease with which these compounds are decomposed in the presence of water makes it difficult to experiment with them. Wislicenus and Menshutkin could not measure the rate constants. Acree and Shadinger found the rate constants for *tertiary*-butyl iodide and bromide very low when treated with sodium 1-phenyl-3-thiourazole. On the other hand, Segaller found that *tertiary*-butyl iodide with sodium phenylate gave an exceedingly rapid rate constant and for all the tertiary halides there appeared to be mostly olefin formed. The value of the rate constant for *tertiary*-amyl iodide showed a large decrease as the reaction proceeded so that the true rate constant was not found. The figure given in table 2 was calculated from the data obtained after the reaction had proceeded for five minutes.

In table 3 some data from the work of Conant and of Hartel, Meer, and Polányi are tabulated to show the effect of the successive replacement of the hydrogen atom by a methyl radical in methyl chloride, and the effect of increasing the number of the $-\text{CH}_2-$ groups in one methyl group. The addition of one, two, or three alkyl radicals greatly increased the speed of the reaction, according to the work of Hartel, Meer, and Polányi, just as the speed increased in going from the lower to the higher members of the primary straight chain halides. On the contrary, in the work of Conant with potassium iodide in acetone, a second methyl group greatly slowed down the rate while a third methyl group had only a slight effect over that of the second group. When successive $-\text{CH}_2-$ groups were introduced into one methyl group a slight increase appeared for the addition of each $-\text{CH}_2-$ group; when five $-\text{CH}_2-$ groups were added, the apparent increase fell off again. The results are not conclusive for the effect of the changes in the structure of the substituted methyl chlorides after the addition of two methyl groups. It is possible that the small

TABLE 2

Rate constants of the primary, secondary, tertiary, and iso halides

WORKER		COMPOUND	PRIMARY	SECONDARY	TERTIARY	ISO
(a) Wislicenus (141)	Time in min.	C ₃ H ₇ I C ₄ H ₉ I	170	450	<3 days	840
(b) Menshutkin (73)	K _{100°} /min.	C ₃ H ₇ I C ₄ H ₉ I	0.0116 0.0083	0.0012		0.0019
(c) Hecht, Conrad and Bruckner (43)	K _{30°} /min.	C ₃ H ₇ I	0.0018	0.0010		
(d) Brussoff (8)	Time in min. for 20 cc.	C ₄ H ₉ I	0.50	2.53	4.00	1.42
(e) Burke and Donnan (9)	K _{24.5°} /min.	C ₄ H ₉ I C ₅ H ₁₁ I	0.00069			0.00138 0.00567
(f) Acree and Shadinger (1)	K _{25°} /min.	C ₃ H ₇ I C ₄ H ₉ I C ₅ H ₁₁ I	0.20 0.214	0.0222	0.00088	0.0085 0.0464
(g) Segaller (101)	K _{42.5°} /min.	C ₃ H ₇ I C ₄ H ₉ I C ₅ H ₁₁ I C ₆ H ₁₃ I C ₇ H ₁₅ I C ₈ H ₁₇ I	0.002788 0.002544 0.001147 0.002436 0.002408 0.002389	0.002238 0.002388 0.002150 0.002029 0.001960 0.001919	0.0661 0.0620	0.000666 0.001211
(h) Lengfeld (64)	Per cent change in 1 day at 18°C.	C ₃ H ₇ Br C ₄ H ₉ Br C ₅ H ₁₁ Br	7.00 6.39	1.67	85.35	2.60 3.62
(i) Long (69)	K _{92.5°} /hr.	C ₃ H ₇ Br C ₄ H ₉ Br C ₅ H ₁₁ Br		0.708		0.0246 0.175

(a) RI + CH₃COCHNaCOOC₂H₅ in acetone.(b) RI + N(C₂H₅)₃ in acetone.(c) RI + NaOC₂H₅ in methyl alcohol.(d) RI + KOC₂H₅.(e) RI + AgNO₃ in alcohol.

(f) RI + Na 1-phenyl-3-thiourazole.

(g) RI + NaOC₂H₅ in alcohol.(h) RBr + KOC₂H₅.(i) RBr + pyridine in iso-C₅H₁₁OH.

(j) RCl + Na(v).

(k) RCl + KI in acetone.

TABLE 2—*Concluded*

WORKER		COMPOUND	PRIMARY	SECOND-ARY	TERTIARY	ISO
(j) Hartel, Meer, and Polányi (41)	$T_{275^{\circ}} \text{ C.}$	$\text{C}_3\text{H}_7\text{Cl}$	4400	3300		
		$\text{C}_4\text{H}_9\text{Cl}$	3300	2200	1500	3500
		$\text{C}_5\text{H}_{11}\text{Cl}$	2200		600	2000
(f) Acree and Shad-inger (1)	$K_{25^{\circ}}/\text{min.}$	$\text{C}_3\text{H}_7\text{Br}$	0.0764	0.0062		
		$\text{C}_4\text{H}_9\text{Br}$	0.0742			0.0064
		$\text{C}_5\text{H}_{11}\text{Br}$				0.0356
(k) Conant (16)	$K_{60^{\circ}}/\text{min.}$	$\text{C}_4\text{H}_9\text{Cl}$	0.101		0.0018	
		$\text{C}_5\text{H}_{11}\text{Cl}$	0.128			0.0678

effect observed is a real one, for since the reactivity of the halide is considered to depend on the resultant of the central carbon atom and the three groups attached to it, the laws governing the resultant might account for the observed effect.

There is further evidence to emphasize this possibility. When three phenyl groups are attached to one carbon atom, the resultant of this grouping is known to show unusual properties. The force between this grouping and the halogen atom seems to be a minimum, as witnessed by the great tendency to form a free radical. Could there not be groupings in alkyl radicals which would show the same tendency though perhaps not so strongly? The action of *tertiary*-butyl and *tertiary*-amyl halides appears irregular. As an example, Lewis (65) found that the *tertiary*-butyl group enters the benzene ring in preference to the side chain when *tertiary*-butyl chloride reacts with phenol to form *tertiary*-butyl phenol. The formation of an ether would have been expected. Also, it is known that when an attempt is made to introduce the isobutyl group into the ring the *tertiary*-butyl isomers are usually formed. Thus evidence points to the fact that some tertiary compounds give rise to unexpected results. If this effect is due to some particular structure formation that gives a necessary resultant condition, it would be expected that a grouping with this structure might show an unusual reaction when combined with one halogen but not with the other halogens. In table 4 some results of Acree and Shadinger are given for the reaction with sodium 1-phenyl-3-thiouazole. In passing from the iodide to the chloride the speed of reaction with the tertiary halide increases as compared to the corresponding primary halide and the corresponding iso halide until the speed of the *tertiary*-butyl chloride is actually greater than the speed of the isobutyl chloride. Obviously, the resultant for the three butyl structures must be a constant for that structure independent of the halogen that is joined to it, so that the actual factor deter-

TABLE 3
Rate constants for some primary, secondary, and tertiary halides

COMPOUND	(a) CONANT (16) $K_{60^\circ/\text{HR.}}$	(b) HARTEL, MEER, AND POLÁNYI (41) $T_{275^\circ\text{C.}}$	COMPOUND	(a) CONANT (16) $K_{60^\circ/\text{HR.}}$	(b) HARTEL, MEER, AND POLÁNYI (41) $T_{275^\circ\text{C.}}$
$\begin{array}{c} \text{CH}_3 \\ \\ \text{H}-\text{CCl} \\ \\ \text{H} \end{array}$	0.1960	7000	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{H} \end{array}$	0.0015	3300
$\begin{array}{c} \text{CH}_2 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{H} \end{array}$	0.0015	3300	$\begin{array}{c} \text{CH}_3\text{CH}_2 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{H} \end{array}$	0.0022	2200
$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{CH}_3 \end{array}$	0.0018	1500	$\begin{array}{c} \text{CH}_3(\text{CH}_2)_2 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{H} \end{array}$	0.0048	
			$\begin{array}{c} \text{CH}_3(\text{CH}_2)_3 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{H} \end{array}$	0.0075	
			$\begin{array}{c} \text{CH}_3(\text{CH}_2)_6 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{H} \end{array}$	0.0026	
			$\begin{array}{c} \text{CH}_3(\text{CH}_2)_2 \\ \\ \text{CH}_3-\text{CCl} \\ \\ \text{CH}_3 \end{array}$	0.0029	600

mining the change in the relative rates between the three butyl structures and the particular halogen must be due to the change in the ratio of the resultant of each butyl structure to each halogen.

Kharasch and coworkers (49-52) have found recently that for the addition reaction between hydrobromic acid and double bond compounds the apparently abnormal results which have been obtained previously are explainable on the basis that the formation of a peroxide form with the double bond compound gives rise to another possible reaction. For propylene, vinyl bromide, allyl bromide, butene-1, and isopropylene the Markownikoff rule was followed, and the formation of an iso compound resulted. On the other hand, when a peroxide was formed the hydrogen of hydrobromic acid added to the double bond carbon atoms, resulting in the formation of a tertiary compound. If it is assumed that the oxygens of the

TABLE 4
Rate constants for the butyl halides using RI and sodium thiourazole
Acree and Shadinger (1)

RADICAL	IODIDE $K_{25^\circ} / \text{MIN}$	BROMIDE $K_{25^\circ} / \text{MIN.}$	CHLORIDE $K_{25^\circ} / \text{MIN.}$
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{—}$	0.21400	0.0740	0.00364
$\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH} \\ \diagdown \\ \text{CH}_3 \end{array} \text{CHCH}_2\text{—}$	0.00850	0.0064	0.00029
$\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH}_2 \\ \diagdown \\ \text{CH}_3 \end{array} \text{—C—}$	0.00088	0.0011	0.00055

peroxide grouping add to the double bond as represented by the structure,
 $\begin{array}{c} \text{—C—C—} \\ | \quad | \\ \text{O} \quad \text{O} \end{array}$, then it follows that the force between these two carbon atoms

has been altered. This, in turn, ought to affect the reactivity of the halogen in vinyl bromide and allyl bromide. Vinyl bromide was found to be more sensitive to the peroxide reaction than allyl bromide; this would be expected from the structure of the two compounds. Should experiments prove that the presence of a peroxide form alters the reactivity of the halogen, the agent which affects some of the apparently unusual reactions of the isobutyl and *tertiary*-butyl halides when present with a double bond will be known, but why in some instances the iso grouping and in other instances the tertiary grouping proves to be the preferential structure has not been explained in any of the existing theories.

The effect of the double bond and the phenyl groups

There are very few data for the vinyl halides. The early work of Wislicenus showed that these compounds reacted too slowly to serve as suitable compounds for experimentation. The vinyl halides may be thought of as methyl halide derivatives in which two hydrogen atoms have been replaced by a double bond and a $-\text{CH}_2-$ group. This double bond causes a decrease in the reactivity of the halide. If, then, the double bond causes a decrease in the reactivity of the simplest carbon halide, it would be expected that the double bond, in general, would cause a decrease in the reactivity of compounds; however, the allyl halogen derivatives, those of the next higher member in the series, were shown to have a greatly increased reactivity. Wislicenus and others concluded that this increased reactivity could not be due to the double bond. In the allyl halides the double bond is not between the α -carbon atom or the carbon atom to which the halogen atom is attached and the β -carbon atom, but between the β - and γ -carbon atoms. If the double bond in the vinyl halides is considered as increasing the force between the carbon atoms and the remaining atoms attached to them, the lessened reactivity would be due to the greater force between the carbon-halogen bond. In the allyl halides the increase in force due to the double bond would be felt in an increase of force by the β -carbon atom for the α -carbon atom. This would result in a decrease in the force between the carbon atom and the halogen, and in turn would bring about an increased reactivity of the halogen. Whatever mechanism is preferred to explain the reactivity of the two types of halides is immaterial in this discussion, as it is sufficient for all purposes here to conclude that when the carbon atom to which a halogen atom is attached holds a double bond, the reactivity of the halide is decreased. If the double bond is one removed from the carbon atom holding the halogen atom, the reactivity of the resulting halide is increased. Table 5 gives data for the allyl and *n*-propyl halides. In every case there is a large increase in the reactivity for the presence of the double bond. The figures in parenthesis have been calculated by the use of temperature data. The values of Segaller for allyl iodide involve a special assumption of normality. The work of Polányi includes the only data which give a value for vinyl chloride. In this case all of Polányi's data fall in line with the data of other workers.

Carothers and coworkers (11-13) have shown that certain compounds possess the tendency to polymerize easily; on account of this property these have been used in the work for the investigation of synthetic rubber. They found that vinyl chloride and bromide polymerized spontaneously. The speed of the bromide was greater than that of the chloride. The reactivities of these halides have been shown to be very low, so that the halogen

TABLE 5
Rate constants for *n*-propyl, allyl, and phenylmethyl halides

WORKER		ALKYL RADICAL	IODIDE	BRO- MIDE	CHLORIDE
(a) Wislicenus (141)	Minimum time in minutes	CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ — C ₆ H ₅ CH ₂ —	170 1	900 18 5	540 36
(b) Hecht, Conrad, and Bruckner (44)	K _{24.5°} /min. K _{0°} /min.	CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ — C ₆ H ₅ CH ₂ —	0.00087 0.04239 0.00446		
(c) Slator (118)	K _{35°} /min.	CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ — C ₆ H ₅ CH ₂ —	0.056 (9.7)		0.166
(d ₁) Preston and Jones (98)	K _{40°} /min.	CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ —	0.0098 3.57		
(d ₂) Preston and Jones (98)		CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ —	0.0076 2 25		
(e) Clarke (14)	K _{55.5°} /hr.	CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ — C ₆ H ₅ CH ₂ —		0.179 1.253 5.118	
(f) Segaller (101)	K _{42.5°} /min.	CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ —	0.00279 (0 5240)		
(g) Thomas (128)	K _{15°} /hr.	CH ₂ =CHCH ₂ — C ₆ H ₅ CH ₂ —		1.08 6.34	
(h) Conant (16, 17)	K _{50°} /hr.	CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ — C ₆ H ₅ CH ₂ —			0.0434 (3.16) (7.89)
(i) Hartel, Meer, and Polányi (41)	T = 275°C.	CH ₂ =CH— CH ₃ CH ₂ CH ₂ — CH ₂ =CHCH ₂ — C ₆ H ₅ CH ₂ —			11000 4400 250 >1

(a) RI + CH₃COCHNaCOOC₂H₅ in alcohol.

(b) RI + NaOC₂H₅.

(c) RI + Na₂S₂O₃ in alcohol + H₂O.

(d₁) RI + (CH₃)₂NC₆H₅ in alcohol.

(d₂) RI + (iso-C₅H₁₁)₃N in alcohol.

(e) RBr + C₆H₅N in alcohol.

(f) RI + C₆H₅ONa in alcohol.

(g) RBr + (CH₃)₂NC₆H₅ in alcohol.

(h) RCl + KI in acetone.

(i) RCl + Na(v).

is very firmly held. Besides holding the halogen securely, the halides exhibit a great tendency to join the molecules end to end. As propylene does not polymerize except with the use of catalysts, polymerization cannot be due only to the double bond. Chloroprene, $\text{CH}_2=\text{C}-\text{CH}=\text{CH}_2$,



polymerized 700 times more readily than isoprene, $\text{CH}_2=\text{C}-\text{CH}=\text{CH}_2$,



or butadiene, $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$. Bromoprene polymerized still more rapidly. The effect of a halogen atom on the β -carbon atom is seen in these two halides. When two halogens are present in the ethane molecule as in dichloro- and dibromo-ethylene, polymerization takes place more rapidly than in the case of vinyl chloride and bromide, according to Staudinger and Feisst (125); and it will be shown later that dichloro- and dibromo-ethylene are not as reactive as the monohalogen derivatives. It was observed by Carothers and coworkers that dichloroprene, $\text{CH}_2=\text{C}-\text{C}=\text{CH}_2$, was found to polymerize faster than bromoprene, and that



while it polymerized ten times faster than chloroprene the product was not rubber-like. The increase in rate of polymerization would be expected, since there are present two $\text{CH}_2=\text{C}-$ groups. The change in the



properties is not surprising, because in some symmetrical compounds there is a tendency for the central $-\text{C}-\text{C}-$ bond to weaken. The presence of three halogens, each one on a different carbon atom, slowed up the rate of polymerization. This would be expected because one $-\text{C}-\text{C}-$ grouping



has been altered by a large factor, the presence of another chlorine atom. Since isoprene and butadiene polymerize so easily, the two $\text{CH}_2=\text{CH}-$ groupings joined together must be a large factor in governing this property. If a chlorine atom is introduced on the end carbon atom in isoprene, the rate of polymerization is not increased and the polymerized product has little strength. Considering only half of this molecule that contains the halogen, it is the reverse of the vinyl halide molecule except for the presence of one hydrogen. But in reversing the grouping the effects due to the particular vinyl structure have been greatly altered. The properties of the resulting compound are what might be anticipated. The presence of a methyl group on the α -carbon atom in methylchloroprene does not affect the rate but does affect the properties. This would follow because the two halves of the molecule have been altered; consequently, the force between

the center carbon-carbon bond has been altered. For compounds of the type $\text{CH}_2=\text{CH}-\text{C}=\text{CHR}$ the rate of polymerization decreases with



increase in the $-\text{CH}_2-$ groups in the R group. This is in accordance with the effect of alkyl groups given above.

The effect of replacement of a hydrogen atom in methyl chloride by a phenyl group is shown by the data given in table 5 to increase greatly the rate of the resulting halide. The tremendous increase in the results of Conant and Kirner (17, 18) for the benzyl chloride as compared to the values of Clarke (14) with pyridine may be justified in the fact that Conant and Kirner used acetone as a solvent. This is known to increase the rates of reaction to a much greater extent than alcohol, which Clarke used. It should be mentioned here that halobenzenes are known to react more slowly than the phenylmethyl halides. The halobenzene compounds involve a consideration of a halogen attached to a ring carbon atom and will not be discussed until later.

The effect of the carboxyl group

The ionization constants for the normal acids of the acetic acid series show only a slight change with increase in the number of $-\text{CH}_2-$ groups present in the alkyl radical. There is a large decrease in going from formic to acetic acid, but beyond acetic acid there is no consistent increase or decrease in passing from member to member of the series, although there is a trend toward a decrease in the rate for the whole series. For the chloroacetic acid series there is a relatively large increase in the ionization constants with the increase in the number of the halogens present, as shown in table 6. From these figures the effect on the force between the oxygen and hydrogen atoms in the carboxyl group must be greatly weakened when a halogen is attached to the carbon adjacent to the carboxyl carbon atom and only slightly affected by the introduction of a $-\text{CH}_2-$ group in the alkyl radical. In considering the effect of a carboxyl group substituted for a hydrogen atom in a methyl halide, it would be expected that the reactivity of the halogen would be increased. This was found to be the case as shown by data given in table 8.

The reactivity of a number of the halogen acids is shown in table 7 in the work of DeBarr (21) and Senter (105-112). By further substituting an alkyl group for one of the two remaining hydrogen atoms attached to the methylene carbon atom, the reactivity of the halogen atom was increased. Ordinarily an increase in the number of alkyl groups held by the carbon atom holding the halogen atom decreases the reactivity of the halogen atom, but in the case of the halogen acids the work of La Mer and Kammer (63) shows that electrostatic interaction is the important

factor. For bimolecular reactions in dilute solutions Debye, Brönsted, La Mer, Euler, and others have shown that the effects produced by the

TABLE 6

Ionization constants of the normal fatty acids and halogen acetic acids

ACID	$K \times 10^5$	ACID	$K \times 10^5$
HCOOH.....	21.4	CH ₃ COOH.....	1.85
CH ₃ COOH.....	1.85	CH ₂ ClCOOH.....	147.0
CH ₃ CH ₂ COOH.....	1.32	CHCl ₂ COOH.....	5140.0
CH ₃ (CH ₂) ₂ COOH.....	1.53	CCl ₃ COOH.....	121000.0
CH ₃ (CH ₂) ₃ COOH.....	1.59		
CH ₃ (CH ₂) ₄ COOH.....	1.46	CH ₃ CHBrCOOH.....	108.0
CH ₃ (CH ₂) ₅ COOH.....	1.4	CH ₂ BrCH ₂ COOH.....	9.8
CH ₃ (CH ₂) ₆ COOH.....	1.44		
CH ₃ (CH ₂) ₇ COOH.....	1.0		

TABLE 7

Rate constants of some halogen substituted acids and salts

ACID	(a) DE BARR (21) PER CENT CHANGE IN 0.5 HR.	(b) SESTER (108) K_{25° /MIN.	
	Chloride	Bromide	
CH ₂ XCOOH.....	4.06	0.0000055	
CH ₃ CHXCOOH.....	4.42	0.00055	
CH ₃ CH ₂ CHXCOOH.....	5.80	0.0025	

SALT	(c) SESTER (106) $K_{52.4^\circ}$ /MIN.	(d) BACKER AND VON MEIS (3) K_{25° /MIN.		
	Bromide	Chloride	Bromide	Iodide
CH ₂ XCOOK.....	0.0065	0.00461	0.454	0.793
CH ₃ CHXCOOK.....	0.0009	0.00016	0.0134	0.0252
CH ₃ CH ₂ CHXCOOK.....	0.0008		0.0045	
CH ₃ (CH ₂) ₂ CHXCOOK.....			0.0023	
CH ₃ (CH ₂) ₃ CHXCOOK.....			0.0015	
CH ₂ XCH ₂ COOK.....		0.00053	0.0205	0.0326

(a) RCHXCOOH + H₂O.

(b) RCHXCOOH + H₂O.

(c) RCHXCOONa + NaOH.

(d) RCHXCOOK + K₂SO₃ + H₂O.

presence of ions may be explained with the aid of the Debye-Hückel limiting law and the Brönsted theory of primary salt effects. The reaction

between ions will be governed by the attracting and repelling electrical forces where the number of collisions will be affected by the nature and the magnitude of the charges and the concentration of the solution. For the reaction between sodium thiosulfate and the halogen propionic acids, La Mer and Kammer have explained the increase in the reaction rate of β -bromopropionic acid over the α -bromopropionic acid on the basis that the more remote position of the halogen atom from the carboxyl ion in the β -bromo acid decreases the intensity of the negative field and permits an easier approach of the negative $S_2O_3^{--}$ ion. The Debye limiting law does not provide for an unsymmetrical distribution of the charges as is

TABLE 8
Rate constants for halogen esters

COMPOUND	(a) CLARKE (14) $K_{55} 6^\circ$ /HR.	(b) SLATOR (118) K_{25° /MIN.		(c) CONANT (16, 18) K_{50° /HR.	COMPOUND	(d) SENDER (108) K_{26° /MIN.
	Bro- mide	Bro- mide	Chlo- ride	Chlo- ride		Bromide
CH_2XCH_3		0.031		0 101		
$CH_2XCH_2CH_3$	0.0179			0.0434		
CH_2XC00H	0.666				$CH_3CHXC00H$	0.0000055
$CH_2XC00CH_3$	0.919	5.85	0.059	10 9	$CH_3CHXC00CH_3$	0 0000077
$CH_2XC00C_2H_5$	1.004	6.4	0 06	68.9	$CH_3CHXC00C_2H_5$..	0.0000085
$CH_2XC00C_3H_7$	0.752				$CH_3CHXC00C_3H_7$	0.0000087
$CH_2XC00C_4H_9$	0.770					
$CH_2XC00C_3H_7$ -iso...	1.048					

(a) $RXCOOR + C_5H_5N$ in alcohol.

(b) $RXCOOR + Na_2S_2O_3$ in alcohol + water.

(c) $RXCOOR + KI$ in acetone.

(d) $RXCOOR + AgNO_3$ in water.

found in the β -halogen acid. La Mer and Kammer have proposed that the Brønsted-Debye equation should be modified to include an orientation factor arising from a negative charge at each end of a chain. They have also shown that the simultaneous hydrolysis of the halogen in the bromopropionic acids takes place to an appreciable extent; this further complicates the study of the halogen acids.

The change in the reactivity of a series of esters with the change in the alkyl radical of the carboxyl group is indicated in the work of Clarke and Senter given in table 8. With the alkyl radical of the carboxyl group changing from methyl to ethyl to propyl Senter's work showed an increase in the reactivity for the change from methyl to ethyl, but from ethyl to

propyl the small increase was not beyond an experimental error, and not too much weight can be placed on the small increase. For the same series the work of Clarke was not consistent within the series beyond the ethyl ester. The values of the propyl and butyl esters are lower than would be expected, although the value of the isopropyl ester fell as would be anticipated. Work of Slator (117-119) and Conant showed an increase for the ethyl ester over the methyl ester. In general, the data indicate that the reactivity of the halogen esters should increase in going from the methyl ester to the higher esters, but that this increase will become less and less between the higher members of the series.

The substitution of an alkyl group in place of a hydrogen atom in a methyl has been shown to decrease the reactivity of the halogen. This effect appears to hold for a series of halides in which a carboxyl group has

TABLE 9
Rate constants for halogen esters

ESTER	(a) SENDER (108) $K_{49.9^\circ}/\text{MIN.}$	(b) SLATOR (118) $K_{35^\circ}/\text{MIN.}$	(c) DRAKE AND MC ELVAIN (25) PER CENT CHANGE IN 1 HR. AT 190°C.
$\text{CH}_2\text{BrCOOC}_2\text{H}_5$	0.0000208		81.8
$\text{CH}_3\text{CHBrCOOC}_2\text{H}_5$	0.0000085	0.085	43.5
$\text{CH}_3\text{CH}_2\text{CHBrCOOC}_2\text{H}_5$	0.0000038	0.022	15.9
$(\text{CH}_3)_2\text{CBrCOOC}_2\text{H}_5$	0.0000062	Small	4.4
$(\text{CH}_3)_2\text{CHCHBrCOOC}_2\text{H}_5$	0.0000022		

(a) $\text{RCHBrCOOC}_2\text{H}_5 + \text{AgNO}_3$ in H_2O .

(b) $\text{RCHBrCOOC}_2\text{H}_5 + \text{Na}_2\text{S}_2\text{O}_3$ in $\text{H}_2\text{O} + \text{C}_2\text{H}_5\text{OH}$.

(c) $\text{RCHBrCOOC}_2\text{H}_5 + \text{C}_6\text{H}_{10}\text{NH}$.

replaced a hydrogen atom of the methyl halide or, as commonly termed, halogen esters. The trend is clearly seen in the data given in table 9, with one exception in the value of $(\text{CH}_3)_2\text{CBrCOOC}_2\text{H}_5$ for Senter's data. This value is somewhat too large in comparison with the value for $\text{CH}_3\text{CHBrCOOC}_2\text{H}_5$ unless it is exhibiting greater reactivity than some tertiary halides are known to show.

The effect of the carbonyl group

In studying the effect of the carbonyl group the same general effect would be expected as shown by the carboxyl group, with the difference due to the absence of the second oxygen atom and the fact that in the carbonyl grouping the alkyl group is joined directly to the carbon atom. Data for the reactivity of this group of compounds are meager. As a class of compounds they are so reactive that only the chlorides have been used to any extent.

In table 10 the available data have been tabulated. It follows from the data that the carbonyl grouping weakens the carbon-halogen bond to a much greater extent than any other grouping. The values for

TABLE 10
Rate constants for organic halogen compounds

COMPOUND	GROUPING	(a) CONANT (16, 18) K_{50° /HR.	(b) CLARKE (14) $K_{55.6^\circ}$ /HR.		(c) SLA- TOR (118) K_{15° /MIN.	(d) HARTEL, MEER, AND POLÁNYI (41) $T = 275^\circ$	(e) PALOMAA (92) K_{15° /MIN.
		Chloride	Bro- mide	Chlo- ride	Chlo- ride	Chlo- ride	Chloride
$\text{CH}_3\text{CH}_2\text{CH}_2\text{X}$	$-\text{CH}_2\text{CH}_2\text{X}$	0.0434	0.0179			4400	
$\text{CH}_2=\text{CHCH}_2\text{X}$	$\text{C}=\text{C}-\text{CH}_2\text{X}$	(3.16)	1.253			250	
$\text{C}_6\text{H}_5\text{CH}_2\text{X}$	 -CH ₂ X	(7.89)	5.118			>1	
$\text{CH}_3\text{COOCH}_2\text{X}$	$-\text{O}-\text{C}(=\text{O})-\text{CH}_2\text{X}$	(10.8)	0.919				
$\text{C}_6\text{H}_5\text{COOCH}_2\text{X}$			1.927				
$\text{CH}_3\text{OCH}_2\text{X}$	$-\text{O}-\text{CH}_2\text{X}$	(36.7)					
$\text{CH}_3\text{COCH}_2\text{X}$	$-\text{C}(=\text{O})-\text{CH}_2\text{X}$	(1428)		0.0686	0.57	10	0.0083
$\text{C}_6\text{H}_5\text{COCH}_2\text{X}$		(4190)	7.269	0.1339	0.65		
ClCOX	$-\text{C}(=\text{O})-\text{X}$						0.055
CH_3COX						100	0.00506
$\text{C}_6\text{H}_5\text{COX}$		(28)					
$\text{C}_6\text{H}_5\text{COOX}$	$-\text{O}-\text{C}(=\text{O})-\text{X}$	(1.05)					
$\text{C}_6\text{H}_5\text{COOCH}_2\text{X}$	$-\text{O}-\text{C}(=\text{O})-\text{CH}_2\text{X}$	(68.9)					

(a) $\text{RCl} + \text{KI}$ in acetone.

(b) $\text{RBr} + \text{C}_6\text{H}_5\text{N}$ in alcohol.

(c) $\text{RI} + \text{Na}_2\text{S}_2\text{O}_3$ in alcohol.

(d) $\text{RCl} + \text{Na}(\gamma)$.

(e) $\text{RCOCl} + \text{CH}_2\text{OHCH}_2\text{Cl}$ in dioxan.

$\text{CH}_3\text{COCH}_2\text{X}$ and $\text{C}_6\text{H}_5\text{COCH}_2\text{X}$ show the same effect as pointed out above for the methyl and phenyl groups.

The data in table 10 have been grouped to show the relative effect due to particular groupings and are too meager to warrant any positive con-

clusions, but they do show the trend in the relative order. There is an apparent inconsistency in the effect due to the C_6H_5- and CH_3COO- groupings in the work of Conant and Clarke. Of particular interest to theoretical considerations is the reactivity of carbonyl chloride, or phosgene, in the work of Palomaa (92), in which the replacement of a methyl group in acetyl chloride by a chlorine atom increases greatly the reactivity of the chlorine atom in the resulting compound, carbonyl chloride.

So far only the effects of the carboxyl and carbonyl groups when they are adjacent to the methylene carbon atom have been studied. It is interesting to consider the few available values of the rate constants for compounds in which the halogen atom is attached to the carbon atom holding the carboxyl or carbonyl groupings. For the present discussion these compounds may be thought of as substituted methyl halides. The structure of the vinyl halides is an example of the double bond in the same relative position. The vinyl halides are very inert, and it follows that the reactivity of the $RCOX$ compounds should be less than that of the $RCOCH_2X$ compounds. The data are in accordance with this.

The effect of a methylene group

The reactivity of characteristic groupings substituted in the methyl halides has been compared with the reactivity of the methyl halides. Sufficient data are available to permit the study of the effect that will result when one or more methylene groups are between the characteristic grouping and the carbon atom holding the halogen. The simplest case has been considered in the study of the effect of the alkyl radicals where it was found that, in general, the presence of a methylene group decreased the reactivity of the halide. In sections II and IV of table 11 the effect of this grouping on the activating group, phenyl, is shown to decrease greatly the activating effect of this group. In the values of Conant and coworkers given in section II, the constant for the second member is less than that of the third member, but a discussion of this value will be left until later. With the exception of the calculated value of the fifth member, there is a consistent decrease in ascending the series. In section I a regular decrease is found for the potassium salts in the work of Backer and von Mels (3), while in the work of Drake and McElvain (24, 25) with the ethyl esters (section III) there is a decrease with the increase in number of methylene groups, but the decrease for the second member appears to be slightly greater than for the third member. Drake and McElvain investigated the mechanism of the reaction of some bromo esters with piperidine. As the interest was in following the course of the reaction rather than in the relative rates of the reaction, the data for the rate constants were not obtained; however, the percentage change in a given time gives a qualita-

TABLE 11

Rate constants for halides with methylene group present

I	II	III
(a) BAKER AND VON MEELS (3) K_{25° /MIN.	COMPOUND	(b) CONANT (17, 18) K_{50° /HR.

VIII		(c) DRAKE AND MO ELVAIN (25) PER CENT CHANGE IN $\frac{1}{\eta}$ HR. AT 100°C	IX		(b) CONANT (17, 18) K_{50}° /HR.	X		(f) PALOMAA (92) K_{15}° /MIN.
COMPOUND			COMPOUND			COMPOUND		
BrCH ₂ COOC ₂ H ₅		81.8	ClCH ₂ COOCH ₃		(10.79)	ClOCC ₂ H ₅		0.0039
BrCH ₂ CH ₂ COOC ₂ H ₅		97.5	ClCH ₂ CH ₂ COOCH ₃		0.0179	ClOCC ₂ H ₅		Inert
BrCH ₂ CH ₂ CH ₂ COOC ₂ H ₅		43.9	ClCH ₂ (CH ₂) ₂ COOCH ₃		1.58	ClOCC ₂ H ₅		0.00168
BrCH ₂ (CH ₂) ₂ CH ₂ COOC ₂ H ₅		36.1				ClOCCl.....		0.055
						ClOCC ₂ H ₅		0.0083
XI		(f) PALOMAA (92) K_{15}° /MIN.	XII		(h) CONANT (17, 18) K_{50}° /HR.	XIII		(g) KIRNER (55) K_{50}° /HR.
COMPOUND			COMPOUND			COMPOUND		
ClCH ₂ COOCH ₃		0.0083	ClCH ₂ COOC ₂ H ₅		(88.9)	ClCH ₂ CH ₂ OC ₆ H ₅		0.0124
ClCOCH ₃		0.00506	ClCH ₂ CH ₂ COOC ₂ H ₅		0.0667*	ClCH ₂ (CH ₂) ₂ OC ₆ H ₅		0.0694
ClCOCH ₂ CH ₃		0.00391	ClCH ₂ (CH ₂) ₂ COOC ₂ H ₅		0.0686*	ClCH ₂ (CH ₂) ₂ OC ₆ H ₅		0.0572
ClCOCH ₂ CH ₂ CH ₃		0.00482	ClCH ₂ (CH ₂) ₂ COOC ₂ H ₅		0.0562*			
XIV		(h) CLARKE (14) K_{55}° 90° /HR.	XV		(g) KIRNER (55) K_{50}° /HR.	XVI		(b) CONANT (17, 18) K_{50}° /HR.
COMPOUND			COMPOUND			COMPOUND		
BrCH ₂ COOC ₆ H ₅		1.927	ClCH ₂ COOC ₆ H ₅		(2.455)	ClCH ₂ COCC ₂ H ₅		(4190)
BrCH ₂ COOCH ₂ C ₆ H ₅		1.211	ClCH ₂ CH ₂ COOC ₆ H ₅		0.0186	ClCH ₂ CH ₂ COCC ₂ H ₅		3.60
BrCH ₂ COOCH ₃		0.919	ClCH ₂ (CH ₂) ₂ COOC ₆ H ₅		(0.0651)*	ClCH ₂ (CH ₂) ₂ COCC ₂ H ₅		(9.27)

(a) RCHXCOOH + K₂SO₄.
 (b) RCl + KI in acetone.
 (c) RCH₂BrCOOK + C₆H₁₁NH₂.

(d) RCl + C₂H₅ONa.
 (e) RCHCOOH + H₂O.
 (f) RCOCl + CH₃OHCH₂Cl in dioxan.

(g) RCl + KI in acetone.
 (h) RBr + C₆H₅N.
 * Average value.

tive measure of the reactivity. It is possible that rate measurements would not show a decrease for the second member.

The series of results for the halogen esters given in section VIII show that the presence of one methylene group increased the rate constant and succeeding methylene groups decreased the rate, although the decrease was not so great as in the case where one hydrogen had been replaced by a methyl group as in the series in section III. Data in section VII show that this replacement of a hydrogen atom by a methyl group greatly decreased the rate constant for the first member of the series, but when a methylene group was between the carboxyl group and the carbon atom holding the halogen, such replacement affected the rate only slightly. Or in other words, the halogen in the position β to an activating group was more reactive than the halogen in the α -position. In contrast to this the data of Conant and coworkers as given in sections IX, XII, XIII, XV, and XVI show the effects for various chloro esters and ether series. In all these series for the member where one methylene group was between the carbon atom holding the halogen atom and the activating group, the rate constant was lower than for the next higher member in the series. The fourth member showed the expected decrease. For the chloro ester series given in section XII this decrease is so very small that it might be only an experimental error. In the work of Conant and coworkers an examination of the data for individual determinations of the constants showed some cases where there was a great variation in the values and in general, there was a falling-off in the constant as the reaction proceeded. These cases are marked with a star in table 11. In these instances the value taken as the value for the rate constant was the average of the varying constants. When the average constant is a value of results differing as much as 15 to 20 per cent among themselves, it is a question how much importance should be placed in a change of 3 per cent in the constant of the different members of a series. Attention should be called to the uncertainties involved in the values of the constants that are enclosed in parentheses. These values are calculated from experimental values obtained at lower temperatures and necessitate an approximation of a value of A , the activation energy. Thus a small error in experimental values may be increased considerably by the calculation.

In sections IX, XIII, XV, and XVI the activating groups are $-\text{COOCH}_3$, $-\text{OC}_6\text{H}_5$, $-\text{COOC}_6\text{H}_5$, and $-\text{COC}_6\text{H}_5$, respectively. For all these series the second member showed a greater decrease than the third member of the series. This is just the reverse of the results of Drake and McElvain for the bromo esters. From this it is concluded that there is something about the structure $\text{XCH}_2\text{CH}_2\text{R}$, where R is an activating group, that is different from other structures. One explanation would be to assume that

in these β -chloro esters the most important factor in determining the reactivity is no longer the resultant of the carbon atom and the three groups attached to it but rather the forces for particular groupings within the compound so compensating each other that they result in producing another point of weakness. This weakness must be large enough to have an effect on the carbon-halogen bond. Thus the resultant force of the ClCH_2CH_2 — group may be nearly equal to the resultant of force of the —COOR group. This explanation arises from the fact that such compounds as hexaphenylethane, and some derivatives where the two triphenylmethyl groups seem to exert a repulsive force for each other, tend to break apart and form the free radical, triphenylmethyl. The difficulty in this explanation is found in the fact that Drake and McElvain found that the reaction rate of ethyl β -bromopropionate is greatly increased rather than decreased as compared with the ethyl bromoacetate. The normal difference in the carbon-chlorine bond and carbon-bromine bond might account for the fact that the carbon-bromine bond weakens in going from ethyl bromoacetate to ethyl bromopropionate, while in the chlorine derivatives the carbon-chlorine bond is strength. The extent of the present data is not sufficient to more than point to some unusual effects with the β -halogen propionates.

The work of Palomaa (92), where an acid chloride was treated with ethylene chlorohydrin in dioxan (see section X), shows the effect of an —OR group, for which in passing to higher alkyl radicals the reactivity increased as in the case of the esters shown in table 8. The decreasing effect of a methylene group is found again for the last two compounds in this section. On the other hand, in section XI the effect of the halogen attached to the carbon atom of the activating group was to decrease the reactivity as has been found for all such cases. The last three values show the effect of the higher alkyl radicals. There is no apparent reason for the lower value of the second member. In section XIV the same deactivating effect of the methylene group is shown when the methylene group is in a more remote position.

In a series of halogen alkyl sulfides the β -chloroethyl sulfides show unusual reactions, according to the work of Bennett (4-6), Kirner (55, 56), and others. With these unusual reactions is associated the well-known vesicant action. But in view of the amount of data that has been published, any discussion which could be given here would be too inadequate to be merited.

The effect of two or more halogens

Two or more halogens in one compound greatly increase the number of possible reactions which might result when these compounds react with

other substances. This makes it very difficult to determine the actual mechanism by which a reaction proceeds, and in consequence these compounds are seldom used in reaction rate measurements. Petrenko (96) has made an interesting qualitative study in which he determined the percentage of the reaction taking place in a given length of time for some polyhalogen methanes and ethanes when treated with a number of basic substances. The different temperatures used and the time of reaction periods makes it difficult to compare them. However, table 12 shows that when two halogen atoms were on different carbon atoms, the rate of reaction towards potassium hydroxide was decreased for the chloride and increased for the bromide and iodide as compared to the monohalogen

TABLE 12
Rate constants for polyhalogen methanes and ethanes
Petrenko (96)

COMPOUND	CHLORIDE PER CENT CHANGE IN $\frac{1}{2}$ HR.			BROMIDE PER CENT CHANGE IN $\frac{1}{2}$ HR.			IODIDE PER CENT CHANGE IN $\frac{1}{2}$ HR.	
	(1) $T = 90^{\circ}\text{C.}$	(2) $T = 90^{\circ}\text{C.}$	(3) $T = 90^{\circ}\text{C.}$	(1) $T = 58^{\circ}\text{C.}$	(3) $T = 58^{\circ}\text{C.}$	(4) $T = 58^{\circ}\text{C.}$	(1) $T = 40^{\circ}\text{C.}$	(4) $T = 40^{\circ}\text{C.}$
$\text{CH}_3\text{CH}_2\text{X} \dots\dots\dots$	55.3			11.1	5.4	9.1	20.0	7.0
$\text{CH}_2\text{XCH}_2\text{X} \dots\dots\dots$	34.4	8.6	2.5	32.0	1.9	1.1	25.0	50.1
$\text{CH}_3\text{CHX}_2 \dots\dots\dots$	7.8	4.4	0.9	6.0	2.8	2.7	6.4*	2.4*
$\text{CHX}_3 \dots\dots\dots$	71.1	10.3	1.4	46.7	1.2	4.0	38.0	18.5
$\text{CX}_4 \dots\dots\dots$	10.3	9.6	3.6	65.7	4.4	25.6		

(1) $\text{RX} + \text{KOH}$ in 95 per cent alcohol.

(2) $\text{RX} + \text{KCN}$ in 95 per cent alcohol.

(3) $\text{RX} + \text{NH}_3$.

(4) $\text{RX} + \text{C}_2\text{H}_5\text{N}$.

* CH_3I_2 .

derivative; with two halogen atoms on the same carbon atom the rate was greatly decreased. Of the tri and tetra bromo- and chloro-methanes, tri-chloromethane was nearly as reactive as ethylene dichloride, while tri-bromomethane was more reactive than ethylene dibromide, and tetrabromomethane was the most reactive of the series. The extreme difference in the rates of the reactions with the various reagents is striking in that it shows that even the order for a series may be reversed when the character of the reagent is greatly changed. As a whole the results are far from conclusive except for the most general trends. Contrary to these results are the results of Hartel, Meer, and Polányi given in table 14. The disagreement in the results may be attributed to the fact that

the data in table 13 are for a gaseous reaction. From the work of Petrenko it appears that the solvent may have a large influence on the rate of the reaction.

In table 14 the results of Backer and von Mels confirm the same trend shown in the work of Petrenko in that for two like halogens on the same carbon atom the rate is decidedly decreased; when two halogens are attached to different carbon atoms, the rate is increased. Since Backer

TABLE 13
Relative reactivities of some polyhalogen paraffin derivatives
Hartel, Meer, and Polányi (41)

(1) COMPOUND	$R_T = 275^\circ$	COMPOUND	$R_T = 275^\circ$
CH_3Cl	10000	$\text{CH}_3\text{CH}_2\text{Cl}$	7000
CH_2Cl_2	900	$\text{CH}_2\text{ClCH}_2\text{Cl}$	800
CHCl_3	100	CH_3CHCl_2	650
CCl_4	25		
$\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$	4400	$\text{CH}_3\text{CHClCH}_3$	3300
$\text{CH}_2\text{ClCH}_2\text{CH}_2\text{Cl}$	1000	$\text{CH}_3\text{CHClCH}_2\text{Cl}$	500
$\text{CH}_3\text{CHClCH}_2\text{Cl}$	500	$\text{CH}_3\text{CCl}_2\text{CH}_3$	180
$\text{CH}_3\text{CH}_2\text{CHCl}_2$	300		

(1) $\text{RCl} + \text{Na(v)}$.

TABLE 14
Rate constants for halogen salts
Backer and von Mels (3)

(a) SALT	$K_{25^\circ/\text{MIN.}}$	SALT	$K_{25^\circ/\text{MIN.}}$
CH_2ClCOOK	0.0046	CHCl_2COOK	0.00012
CH_2BrCOOK	0.454	CHBrClCOOK	0.0033
$\text{CH}_3\text{CHBrCOOK}$	0.0134	CHBr_2COOK	0.002
$\text{CH}_2\text{BrCH}_2\text{COOK}$	0.0205	$\text{CH}_3\text{CBBr}_2\text{COOK}$	0.0002
		$\text{CH}_2\text{BrCHBrCOOK}$	0.032

(a) $\text{CH}_2\text{XCOOK} + \text{K}_2\text{SO}_3$.

and von Mels used potassium sulfite and Petrenko used potassium hydroxide for reacting substances, one would expect the same effect to be observed in both results; this was confirmed. Of special interest is the value for the potassium salt of chlorobromoacetic acid where the deactivating effect of two halogens on the same atom is almost lost owing to the presence of two unlike halogens.

van Duin (129-131) measured the rate of reaction for a series of substi-

tuted derivatives of ethylene dibromide with potassium iodide in 95 per cent alcohol in which the effect of one activating and then two activating groups may be observed. In table 15 the relative order for the activating groups in the presence of two bromine atoms follows the order given above for one halogen, but with one variation. The order of the rate constants for the methyl and ethyl esters is reversed; moreover, the order of this series agrees with the order given in the work of Clarke with pyridine and not with the order given in the work of Conant with potassium iodide, in that the phenyl group produces greater reactivity than the carbethoxyl group. The dibromosuccinic acids show the effect of a compound with two sym-

TABLE 15
Rate constants for some ethylene dibromides
van Duin (131)

(a) COMPOUND	$K_{25^\circ}/\text{MIN. IN } \frac{1}{2}\text{N KI}$	$K_{25^\circ}/\text{MIN. IN N KI}$
$\text{CH}_2\text{BrCH}_2\text{Br}$	0.000388	0.000150
$\text{CH}_2\text{BrCHBrCOOH}$	0.000686	0.000317
$\text{CH}_2\text{BrCHBrCOOC}_2\text{H}_5$	0.00102	0.000399
$\text{C}_6\text{H}_5\text{CHBrCH}_2\text{Br}$	0.00132	0.000524
$(\text{CH}_3)_2\text{CBrCHBrCOCH}_3$	0.00659	0.00241
$\text{C}_6\text{H}_5\text{CHBrCHBrCOOH}$	0.0240	0.0120
$\text{C}_6\text{H}_5\text{CHBrCHBrCOOCH}_3$	0.0433	0.0170
$\text{C}_6\text{H}_5\text{CHBrCHBrCOOC}_2\text{H}_5$	0.0300	0.0122
$\text{C}_6\text{H}_5\text{CHBrCHBrCOCH}_3$	0.0677	0.0267
Meso $(\text{CHBrCOOH})_2$	0.00103	0.000548
Racemic $(\text{CHBrCOOH})_2$	0.000084	0.0000336
$\text{C}_6\text{H}_5\text{CHBrCHBr}_2$	0.000179	0.0000696
$\text{CHBr}_2\text{CHBr}_2$	0.0000013	0.00000045

(a) $\text{CH}_2\text{BrCH}_2\text{Br} + \text{KI}$ in 95 per cent alcohol.

metrical parts of the molecule. The reactivity of the halogen atom in such compounds is reduced greatly. It would be expected that in this type of compounds the center carbon-carbon bond has been weakened. In this work of van Duin ethylene dibromide and derivatives of it were treated with potassium iodide; the trends for two halogen atoms on the same and on different carbon atoms were the same as those in which similar potassium compounds were the reacting substances. Rate constants for two concentrations are given in table 15. The same relative order is followed with both concentrations except in three instances. It is not clear whether the changes in these instances are real or due to some error in the experimental work.

The reactivity of some tertiary halides

Certain groups have been shown to act as activating groups, while others act as deactivating groups. It would follow that if two or three such groups were present, the effect ought to be doubled or tripled provided that this group is the only governing factor and the effect of each group is merely an additive function. There are no indications that reactivity functions are simple additive relationships. Against the merely doubled or tripled effect of two or three groups would be the effect of primary, secondary, and tertiary compounds. It has been found convenient here to consider the factor governing the reactivity of the halogen as the resultant of the force of the carbon atom holding the halogen and the three groups attached to it. It is conceivable that the force of the resultant of certain groupings will be nearly equal to the force about the halogen atom, a condition which would result in the appearance of unusual reactivity of the halogen. In the case of the secondary compounds where there are two activating groups, the reactivity ought to be somewhat increased, since there is still one hydrogen atom present. The effect of a hydrogen atom has always appeared to be distinctly different from the effect of an alkyl or aryl group; however, for tertiary groupings where there are three activating groups and no hydrogen atom attached to the central carbon atom, the three groupings, which may be similar or nearly similar to each other, would be expected to give rise to unusual inertness or unusual reactivity. The former type is seen in the case of the alkyl halides. In data which have been given above, the alkyl group in itself has been shown to be a deactivating group. It is of interest now to study the effect of three activating groups, either alike or unlike.

Conant and coworkers have found that ethyl acetate is much more reactive than phenylchloromethane, while Clarke and van Duin have found the reverse to be true as shown in table 16. From Conant's data for the relative rates it would be expected that the di- and tri-carbethoxyl groups would increase the activity more than the di- and tri-phenyl groups; that is what they found for the dicarbethoxy- and triphenylmethyl chlorides. In their work there was a large variation in the experimental reaction rate constants for each of these compounds. The triphenylmethyl chloride constants varied from 9.95 to 6.39, while the constants for chloromalonate ester varied from 16.4 to 9.8. These results were considered only preliminary by the authors.

On the basis of the results of Conant, Carothers (10) has made a qualitative study of the phenyl and carbomethoxybromomethanes, namely, $(C_6H_5)_3CBr$ (I), $(C_6H_5)_2CBr(COOCH_3)$ (II), $(C_6H_5)CBr(COOCH_3)_2$ (III), and $CBr(COOCH_3)_3$ (IV) as given in table 17. Toward silver in acetonitrile and in methyl alcohol the order was not given by the predictions of

Conant's result, but would follow according to the results of Clarke and van Duin. Assuming from the tendency to form free radicals that the force of the resultant of the three phenyl groups and the carbon atom to

TABLE 16
Rate constants of mono-, di-, and tri-halides

COMPOUND	(a) CONANT (18) $K_{50^\circ/\text{HR.}}$	(b) CLARKE (14) $K_{55.6^\circ/\text{HR.}}$	(c) VAN DUIN (131) $K_{25^\circ/\text{MIN.}}$
	Chloride	Bromide	Dibromide
$\text{C}_2\text{H}_5\text{COOCH}_2\text{X}$	(68.9)	1.004	0.00102
$\text{C}_6\text{H}_5\text{CH}_2\text{X}$	(7.89)	5.118	0.00132
$(\text{C}_2\text{H}_5\text{COO})_2\text{CHX}$	(2420)*		
$(\text{C}_6\text{H}_5)_3\text{CX}$	(1520)*		

(a) $\text{RCl} + \text{KI}$ in acetone.

(b) $\text{RBr} + \text{C}_6\text{H}_5\text{N}$ in alcohol.

(c) $\text{RCHBrCH}_2\text{Br} + \text{KI}$ in alcohol.

* Average value.

TABLE 17
Relative reactivities of some tertiary bromides
Carothers (10)

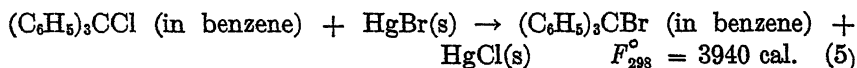
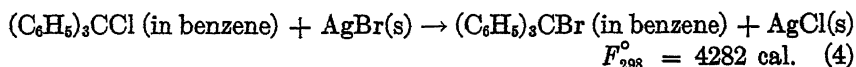
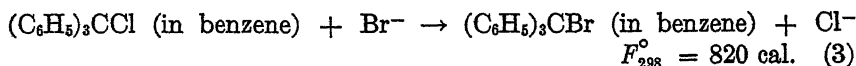
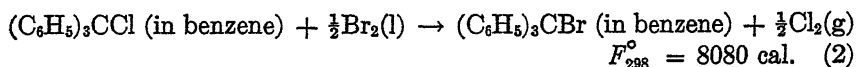
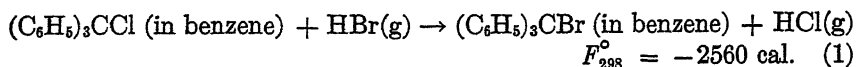
SUBSTANCE	0.1 N AgNO_3 IN ABSOLUTE CH_3CN AT ROOM TEMPERATURE	0.1 N AgNO_3 IN ABSOLUTE CH_3OH	KSCN IN ABSOLUTE CH_3COCH_3
$(\text{C}_6\text{H}_5)_3\text{CBr}$	Instantaneous precipitate	Instantaneous re- action in the cold	Immediate copi- ous precipitate of KBr
$(\text{C}_6\text{H}_5)_2\text{CBr}(\text{COOCH}_3)$	Very rapid pre- cipitate	Reaction 50 per cent complete in 15 min. at room tempera- ture	Slight precipitate in 5 hours
$(\text{C}_6\text{H}_5)\text{CBr}(\text{COOCH}_3)_2$	Slight precipitate in 1 week	Action of boiling NaOCH_3 rapid	Slight precipitate in 5 hours. Some decompo- sition
$\text{CBr}(\text{COOCH}_3)_3$	No precipitate in 3 months	Action of boiling NaOCH_3 very slow	Slight precipitate in 1 hour

which they are attached in triphenylmethyl chloride or bromide is nearly equal to the force of the halogen atom, and assuming from the reactivities that the force of the carbomethoxyl group is not equal to that of the phenyl

group, it would follow that the substitution of one, two, or three carbomethoxyl groups in place of the phenyl group would so alter the resultant in the resulting compound that the reactivity would be decreased. Thus only tertiary halides in which the force of the resultant is nearly equal to the force of the halogen atom will show great reactivity. According to the work of Clarke and van Duin the relative order of I, II, III, and IV for the above series would be expected when the forces of the reagent with which they are treated and the solvent do not induce another field of force. According to the results in table 17, when the halides were treated with potassium sulfocyanide in acetone, the order changed to I, IV, II, and III. In this case the reagent has been changed considerably in character, and the solvent is one which is known to induce greater reactivity. It is reasonable to conclude that the fields of force about the bromine atom have been so altered by these changes that they approach more nearly the resultant of the forces for the $-\text{C}(\text{COOCH}_3)_3$ grouping. As the effects are measured in a qualitative way, any difference in the rate of reaction of the triphenylmethyl bromide with potassium sulfocyanide was not sufficiently marked to be observed or the effect of the induced field is too small in the case of this halide to be reflected in the reactivity. Carothers has pointed out that *tertiary*-butyl chloride reacted instantaneously with silver nitrate in acetonitrile but very slowly with potassium sulfocyanide. In general, the reactivity of the *tertiary*-butyl bromide is not as great as that of the triphenylmethyl bromide, so that there must be a greater force between the resultant and the bromine atom for the *tertiary*-butyl group than for the triphenylmethyl group. The change in the reactivity could be attributed again to the induced field from the reagent and the solvent. The fact that *tertiary*-butyl chloride reacted like triphenylmethyl chloride towards water but not towards calcium bromide could be explained in the same manner.

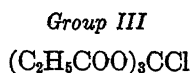
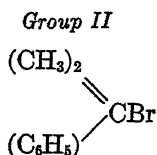
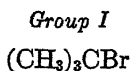
From a thermodynamic study Halford (38) has indicated that triphenylmethyl bromide in benzene dissociates into free radical 10^6 times more readily than the chloride, while the bromide in benzene also has a slightly greater tendency to dissociate into ions than the chloride. Apparently, the relative force with which a halogen atom is held to a carbon atom is not associated chiefly with the question of ionization. Of equal or greater importance is the force between the halogen atom and the resultant of the rest of the molecule, which in some cases becomes repulsive, resulting in the formation of free radicals. According to Straus (127) triphenylmethyl chloride reacted with hydrobromic acid to form triphenylmethyl bromide with the reaction going to 85 per cent of completion. Also triphenylmethyl chloride reacted readily with calcium bromide. Halford has investigated the first reaction and the reaction of triphenylmethyl chloride with bro-

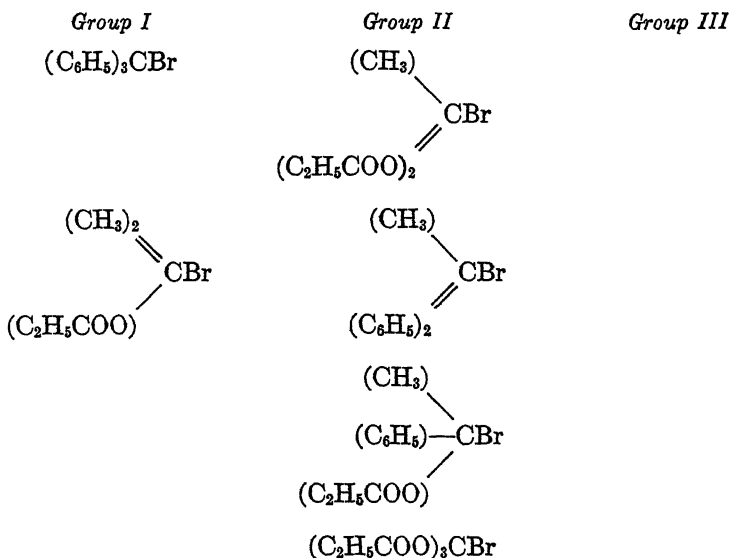
mine, with bromide ion, with solid silver bromide, and with solid mercury bromide. The free energy has been determined for each reaction and is shown below.



Straus found reaction 1 to proceed to the right almost to completion; Halford states that the reaction will probably proceed in either direction because of the ease with which a stream of gas from a generator will carry away the gas which is formed. Equation 3 indicates that for the reaction with bromide or chloride ions the reaction will not tend to go to completion, but equations 4 and 5 indicate that the reaction with silver and mercury chlorides will proceed to completion. This study gives further evidence that the reactivity of some tertiary halogens may be closely linked with the relative ability to form free radicals.

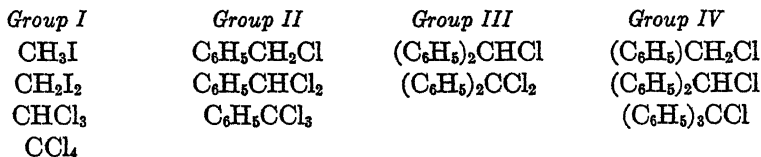
The work of Werner (137), using the series triphenylmethyl, diphenylbenzoylmethyl, phenyldibenzoylmethyl, and tribenzoylmethyl halides with alcohol, gave qualitative results of the same nature as the work of Carothers with the phenylcarbomethoxy halides and silver nitrate. The first three members of the series reacted, the triphenylmethyl being the most reactive; the last member, tribenzoylmethyl halide, gave no reaction. Wheeler and Johnson (139) investigated qualitatively the reaction of a number of tertiary halides of various combinations of methyl, phenyl, carbomethoxyl, and carbethoxyl groups with potassium sulfocyanide. These are listed below.





The halides in the first group reacted smoothly, while those in the second group reacted somewhat more rapidly than the first group. On the other hand, the triethoxymethyl chloride did not react. This agrees with the work of Carothers for the corresponding carbomethoxymethyl bromides. The reaction of this series leads to the idea that the resultant force might not have to be exactly equal to the force of the halogen atom but might be nearly equal to the force of the halogen atom and yet permit the tertiary halide to show unusual reactivity. Such a relationship would allow for a small variation in the resultant when the activating groups are not too different in activating ability. Since three methyl groups are present in the *tertiary*-butyl halides, these halides might be called a special case where the alkyl group acts as an activating group. There is no definite measure of the force of the various groups, so that present data do not tell whether tribenzoylmethyl bromide would be reactive towards silver nitrate.

Further evidence of the unusual features of some phenyl halides was observed in the work of Staudinger, Clar, and Czako (124), who treated the substances listed below with zinc and found that only the last member of groups II, III, and IV reacted. The triphenylmethyl chloride reacted more readily than did the trichlorophenylmethane.



The effect of substitution in the benzene ring

The preceding discussion has considered only the effect of the unsubstituted benzene ring. The reactivity of the halogen when attached to a carbon atom of the ring is known to be very small. Apparently, the forces about each of the six carbon atoms in benzene have been greatly modified by the close proximity of the other atoms, with the result that one halogen is held rather securely when it is attached to a ring carbon atom. Since the forces in the ring structure are a function of the distance between the atoms, the various positions at which substituents are attached to the carbon atoms would be expected to produce different effects on the strength with which the carbon atom holds the reacting halogen atom. The qualitative work of Klages and Liecke (57, 58), in which the benzene halides were treated with hydrogen iodide, makes clear the fact that the reactivity of the halogen attached to a carbon atom in the benzene ring is a function of the particular halogen, the number of halogen atoms, and the position of the various halogen atoms in the ring.

The phenyl group substituted in the methyl halides has been shown to increase greatly the reactivity of the halogen atom. It follows that the effect of the various groupings held by the ring carbon atoms of the phenyl group which is substituted in a methyl halide or derivative should be sufficient in magnitude to enable the study of the different aspects associated with substitution in the benzene ring. Several studies have been made in which the parent substances have been benzyl halides, benzoyl chlorides, and phenol derivatives. Benzoyl chloride and derivatives would be expected to react more rapidly than the benzyl halides, because of the oxygen atom attached to the central carbon atom holding the reacting halogen. This difference has been observed. In these substances the substituted phenyl group is close enough to the halogen atom in the side chain for the force fields of the ring to produce marked effects on the force about the halogen atom and in turn on the reactivity of the halogen. With no mathematical knowledge about the fields of force, one finds the study a very complex one with more apparent contradictions than agreements. These contradictions are in a large measure, no doubt, due to the fact that the nature of the reagent and solvent used for the particular study now exerts a larger effect than for the work previously considered. There are tabulated in table 18 the results that are available for the above types of reactions. Only a few generalizations are permissible. When the force fields of the methyl halide with the exclusion of the phenyl group and the reacting substance are weak compared to the cumulated effects of the force fields of the phenyl ring and the substituents in the ring, substituents with strong fields of force decrease the reactivity of the side-chain halogen atom, while substituents with weak fields of force increase the reactivity of the

TABLE 18
 Rate constants of some benzene derivatives

SUBSTITUENT IN RING	(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)	(i)	(j)
	CONANT (17, 18) $K_{50^\circ}/\text{hr.}$	OLIVIER (88, 89) $K_{33^\circ}/\text{min.}$	NORRIS (83, 84) $K_{25^\circ}/\text{min.}$	FRANZEN AND ROSENBERG (31) $K_{30^\circ}/\text{min.}$	PRESTON AND JONES (98) $K_{40^\circ}/\text{min.}$	PRESTON AND JONES (98) $K_{40^\circ}/\text{min.}$	GOLDS- WORTHY (35) $K_{42.5^\circ}/\text{min.}$	NORRIS (86) $K_{28^\circ}/\text{min.}$	OLIVIER (90) $K_0/\text{min.}$	SLATOR (118) $K_{35^\circ}/\text{min.}$
None.....	7 89	0 0155	0 00266	6 4			0 00702	0 00365	0 026	
<i>o</i> -ClC ₆ H ₄	28.7	0 0055	0 0000254	7.0			0 00334	0 038	0 038	
<i>m</i> -ClC ₆ H ₄		0 00368	0 0000593	8.8			0 00278	0 038	0 038	
<i>p</i> -ClC ₆ H ₄	22.1	0 0096	0 00107	12.5			0 00393	0 00559	0 022	
<i>o</i> -BrC ₆ H ₄	3092.0	0 0044		6.2					0 035	
<i>m</i> -BrC ₆ H ₄		0 0033		9.1					0 044	
<i>p</i> -BrC ₆ H ₄	1925.0	0 0078	0 000838		6.03	1 5		0 00650	0 024	
<i>o</i> -IC ₆ H ₄		0 0044								
<i>m</i> -IC ₆ H ₄		0 0031								
<i>p</i> -IC ₆ H ₄		0 0074								
		$K_{30^\circ}/\text{min.}$								
<i>o</i> -NO ₂ C ₆ H ₄	72.9	0 0000063						0 00528		0 166
<i>m</i> -NO ₂ C ₆ H ₄	31.4	0 0000052						0 00694	0 046	0 194
<i>p</i> -NO ₂ C ₆ H ₄	55.1	0 0000049						0 0036	0 030	0 305
		$K_{33^\circ}/\text{min.}$								
<i>o</i> -CH ₃ C ₆ H ₄		0 075	0 00764		13.2	3.4				
<i>m</i> -CH ₃ C ₆ H ₄		0 0216	0 00554		8.62	2.7			0 038	
<i>p</i> -CH ₃ C ₆ H ₄		0 164	0 0433		23.2	6.8		0 00235	0 075	

- (a) C₆H₅CH₂Cl + KI in acetone.
 (b) C₆H₅CH₂Cl + C₂H₅OH and H₂O.
 (c) C₆H₅CH(C₆H₅)Cl + C₂H₅OH.
 (d) C₆H₅CH₂Cl + NaOC₂H₅.
 (e) CH₃C₆H₄CH₂Br + (CH₃)₂NC₆H₅.
 (f) CH₃C₆H₄CH₂Br + (iso-C₆H₁₁)₂N.
 (g) C₆H₅ONa + C₂H₅I in C₂H₅OH.
 (h) C₆H₅COC(=O)Cl + iso-C₃H₇OH.
 (i) C₆H₅COC(=O)Cl + (CH₃)₂CO in H₂O.
 (j) C₆H₅CH₂Cl + Na₂S₂O₃ in C₂H₅OH + H₂O.

side-chain halogen atom. The effect of distance is seen in the case of the ortho-, meta-, and para-isomers, where for substituents which cause a decrease in the reactivity of a methyl halide the para-isomer produces the least decrease, and for substituents which cause an increase in reactivity of a methyl halide, the para-isomer produces the greatest increase. The tremendous effect of the nature of the reacting substance throughout all the results in table 18 is evident; especially, the effect of the various amines is outstanding in the work of Preston and Jones (98) shown in table 18 and of Rhineland (99) shown in table 20, as well as in the work of Menschutkin (75) and of Moore, Somerville, and Derry (80). In this connection

TABLE 19
Rate constants of some benzene derivatives

(a) BRADFIELD AND JONES (7)		(b) NORRIS AND COWORKERS (83, 84)	
Compound	$K_{20^\circ}/\text{min.}$	Compound	$K_{25^\circ}/\text{min.}$
$p\text{-CH}_3\text{OC}_6\text{H}_4\text{Cl}$	1.226	$\text{C}_6\text{H}_5\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$	0.00266
$p\text{-C}_2\text{H}_5\text{OC}_6\text{H}_4\text{Cl}$	2.443	$p\text{-CH}_3\text{C}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$	0.0433
$p\text{-C}_2\text{H}_7\text{OC}_6\text{H}_4\text{Cl}$	2.756	$p\text{-C}_2\text{H}_5\text{C}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$	0.0558
$p\text{-iso-C}_3\text{H}_7\text{OC}_6\text{H}_4\text{Cl}$	5.377	$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$	0.0362
$p\text{-C}_6\text{H}_5\text{OC}_6\text{H}_4\text{Cl}$	2.723	$o\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$	0.247
$p\text{-C}_6\text{H}_5\text{CH}_2\text{OC}_6\text{H}_4\text{Cl}$	0.8371	$p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$	Large
$p\text{-ClC}_6\text{H}_4\text{CH}_2\text{OC}_6\text{H}_4\text{Cl}$	0.4834	$p\text{-C}_6\text{H}_5\text{OC}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$...	0.843
$p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{OC}_6\text{H}_4\text{Cl}$	0.1742	$p, p'-(\text{CH}_3)_2(\text{C}_6\text{H}_4)_2\text{CHCl}$	1.10
$m\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{OC}_6\text{H}_4\text{Cl}$	0.2104	$p, p'-(\text{Cl}_2)(\text{C}_6\text{H}_4)_2\text{CHCl}$	0.004
$o\text{-CH}_3\text{OC}_6\text{H}_4\text{Cl}$	4.441		
$o\text{-C}_2\text{H}_5\text{OC}_6\text{H}_4\text{Cl}$	8.873		
$o\text{-(p-NO}_2\text{C}_6\text{H}_4\text{O)C}_6\text{H}_4\text{Cl}$	0.6417		

(a) $\text{ROC}_6\text{H}_4\text{Cl} + \text{Cl}_2$ in 99.5 per cent acetic acid.

(b) $\text{RC}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl} + \text{C}_2\text{H}_5\text{OH}$.

it might be recalled that, according to the work of Moelwyn-Hughes, most of the reactions belonging to the second class of substances that react at a slower rate than the collision theory predicts involve nitrogen compounds.

The relative influence of the various groups pointed out above in the case of the derivatives of methyl halides, can be seen to hold when the same substituents are found in the ring. Thus in the work of Bradfield and Jones (7) and of Norris (83-87) given in table 19 for the alkyl group which is a deactivating group of the methyl derivatives, the reactivity is increased consistently in going to the higher alkyl groups, while the phenyl group, an activating group, decreases the reactivity when substituted in the phenyl ring. The same effects are observed for an R group when it is not

TABLE 20
 Rate constants of some benzene derivatives

COMPOUND	(a)	(b)	(c)	COMPOUND	(c)
	HOLLEMAN AND VAN HAEF- TEN (46) $K_{60^\circ}/\text{MIN.}$	DE MOOY (23) $K_{85^\circ}/\text{HR.}$	OLIVIER (88) $K_{40.4^\circ}/\text{MIN.}$		OLIVIER (88) $K_{60^\circ}/\text{MIN.}$
<i>o</i> -NO ₂ C ₆ H ₄ Cl.....	0.000000245	0.369	0.0000184	2,6-Br ₂ C ₆ H ₃ CH ₂ Cl..	0.000095
<i>m</i> -NO ₂ C ₆ H ₄ Cl.....			0.0000212	2,4-Br ₂ C ₆ H ₃ CH ₂ Cl..	0.000055
<i>p</i> -NO ₂ C ₆ H ₄ Cl.....	0.000000987	1.39	0.0000168	3,5-Br ₂ C ₆ H ₃ CH ₂ Cl..	0.000032
1,2-(NO ₂) ₂ C ₆ H ₃ Cl-4..	0.110				(d)
1,4-(NO ₂) ₂ C ₆ H ₃ Cl-3..	0.0331				OLIVIER
1,5-(NO ₂) ₂ C ₆ H ₃ Cl-2..	0.0318				(88)
1,3-(NO ₂) ₂ C ₆ H ₃ Cl-2..	0.0074				$K_{60^\circ}/\text{MIN.}$
1,6-(NO ₂) ₂ C ₆ H ₃ Cl-2..	0.0029				
1,3-Cl ₂ C ₆ H ₃ NO ₂ -4...	0.0000183	17.42		2,6-Br ₂ C ₆ H ₃ COCl..	0.00029
1,2-Cl ₂ C ₆ H ₃ NO ₂ -4...	0.0000170	19.41*		2,4-Br ₂ C ₆ H ₃ COCl..	0.057
1,5-Cl ₂ C ₆ H ₃ NO ₂ -2...	0.00000297	3.93		3,5-Br ₂ C ₆ H ₃ COCl..	0.35
1,3-Cl ₂ C ₆ H ₃ NO ₂ -2...	0.00000131	1.74			
1,6-Cl ₂ C ₆ H ₃ NO ₂ -2...	0.000000395	0.135			
1,3,5-Cl ₃ C ₆ H ₂ NO ₂ -4..	0.000360				
1,2,5-Cl ₃ C ₆ H ₂ NO ₂ -4..	0.000283				
1,3,5-Cl ₃ C ₆ H ₂ NO ₂ -2..	0.000033				
1,3,4-Cl ₃ C ₆ H ₂ NO ₂ -2..	0.000030				
1,4,6-Cl ₃ C ₆ H ₂ NO ₂ -2..	0.0000042				
1,5,6-Cl ₃ C ₆ H ₂ NO ₂ -2..	0.0000016				

COMPOUND	(e)	COMPOUND	(f)	(g)
	LUCOFF (70) $K_{15^\circ}/\text{MIN.}$		RHINELANDER (99) $K_{50^\circ}/\text{HR.}$	
			C ₆ H ₅ NH ₂	C ₆ H ₅ NHCH ₃
<i>o</i> -(NO ₂) ₂ C ₆ H ₃ Cl.....	0.003	<i>o</i> -(NO ₂)C ₆ H ₄ Br.....	0.0000627	0.0000271
<i>p</i> -(NO ₂) ₂ C ₆ H ₃ Cl.....	0.012	<i>p</i> -(NO ₂)C ₆ H ₄ Br.....	0.000122	0.0000820
2,4-(NO ₂) ₂ C ₆ H ₃ Cl.....	2.94	2,4-(NO ₂) ₂ C ₆ H ₃ Cl.....	0.00275	0.000295
2,4-(NO ₂) ₂ C ₆ H ₃ Br.....	1.89	2,4-(NO ₂) ₂ C ₆ H ₃ Br.....	0.00421	0.000869
2,4-(NO ₂) ₂ C ₆ H ₃ I.....	0.455	2,4-(NO ₂) ₂ C ₆ H ₃ I.....	0.00123	0.000212
		2,4,6-(NO ₂) ₃ C ₆ H ₂ Cl....	0.0190	0.000493
		2,4,6-(NO ₂) ₃ C ₆ H ₂ Br....	0.0331	0.000269
		2,4,6-(NO ₂) ₃ C ₆ H ₂ I....	0.0172	0.000668

 (a) Cl₂C₆H₃NO₂ + NaOCH₃.

 (b) Cl₂C₆H₃NO₂ + NaOCH₃.

 (c) Br₂C₆H₃CH₂Cl + C₂H₅OH.

 (d) Br₂C₆H₃COCl + (CH₃)₂CO + H₂O.

 (e) (NO₂)₂C₆H₃X + C₂H₅OH.

 (f) (NO₂)₂C₆H₃X + C₆H₅NH₂.

 (g) (NO₂)₂C₆H₃X + C₆H₅NHCH₃.

 * 1,4-Cl₂C₆H₃(NO₂)-2

substituted directly into the phenyl group but indirectly through an oxygen atom or as in ether.

The substitution of the nitro group with very strong force fields in the ring increased the reactivity of a ring halogen atom sufficiently to make measurements on these derivatives of benzene. The data tabulated in table 20 show that while one nitro group increased the reactivity of the chlorine atom, two nitro groups increased it very much more. In the case where there were two chlorine atoms and one nitro group present, the second chlorine atom annulled the effect of the nitro group to a large extent. A third chlorine atom, on the other hand, seemed to annul the effect of the second chlorine atom. The positions of the chlorine atoms and the nitro group affected markedly the reactivity, and in general, it appeared that the more closely these groups were located on adjacent carbon atoms the less the effect of one group was observed. The work of Olivier (88-91) given in table 20 shows the effect of the $-\text{CH}_2\text{Cl}$ and $-\text{COCl}$ groups, in which the order of the effect produced in the reactivity by the bromine atoms in the ring has been reversed by the character of the side chain.

SOME PHYSICAL RELATIONSHIPS OF THE ORGANIC HALIDES

A relationship between the structure of an organic halide and its reactivity has been developed by the use of the concept that the force between the halogen atom and the carbon atom will be determined by the resultant of the forces of the carbon atom holding the halogen atom and the remaining three atoms or groups attached to the carbon atom. This concept is so beautifully general that it tells little. No doubt its merit lies in its aid to a clearer understanding of the relationships that have been developed. An attempt has been made throughout this entire discussion to avoid the perplexing aspect of the mechanism of the reaction and, in turn, the various theories of negativity, alternate polarity, induced polarity, positive halogens, affinity, and the like as proposed by Kharasch, Flurschiem, Lapworth, Olivier, Ingold-Patel, Nathan and Watson, Hixon, and others. It may be said that all these theories have their advantages. It would be desirable to relate some physical properties to the reactivities of the halides and the ideas of force fields which have been used. Since the dipole moments deal with electric forces, these will be compared with reactivities. Moreover, some recent experimental work tends to support the concept.

The halides are dipoles. Since a dipole moment is a measure of the electrical unsymmetry, a comparison of the trends in the electric moments with the trends in reactivity ought to give some idea as to whether the reactivity of a halide appears to be a simple function of electrical unsymmetry. Debye has called attention to the fact that although the carbon-hydrogen bond in itself is polar, methane is non-polar, as the spatial con-

figuration of the four carbon-hydrogen bonds gives a resultant of zero. Further, it follows that the aliphatic hydrocarbons should be non-polar; Smyth has found this to be the case for the isomers of heptane. Since the alkyl groups in the isomeric heptanes appear to have no electric moments, all the alkyl halides should have the same electric moments for the same halogen. In table 21 the electric moments of several alkyl chlorides, bromides, and iodides are given. There are small variations between the different halides of a given alkyl group, but these variations are not greater than the variations between the different alkyl members for one halogen. Though it might be conceivable that the electric moments of the alkyl

TABLE 21
Electric moments as $\mu \times 10^{18}$ of some alkyl halides

ALKYL GROUP	CHLO- RIDE	BROMIDE	IODIDE	ALKYL GROUP	CHLO- RIDE	BROMIDE	IODIDE
H.....	1.03	0.79	0.38	C ₇ H ₁₅ X-1.....	1.85	1.84	1.84
CH ₃	1.85	1.50	1.30	C ₇ H ₁₅ X-2.....	2.03	2.06	
C ₂ H ₅	1.99	1.83	1.66	C ₇ H ₁₅ X-3.....	2.04	2.04	1.93
C ₃ H ₇	2.00	1.80	1.60	C ₇ H ₁₅ X-4.....	2.04	2.04	
C ₄ H ₉	1.95	1.97	1.88	<i>n</i> -C ₄ H ₉	1.97	1.97	1.88
C ₇ H ₁₅	1.85	1.84	1.84	<i>iso</i> -C ₄ H ₉	1.97	1.96	1.87
C ₈ H ₁₇	1.52	1.50	1.25	<i>sec</i> -C ₄ H ₉	2.12	2.09	2.04
				<i>tert</i> -C ₄ H ₉	2.21	2.15	2.13
CH ₃ Cl.....	1.86	CH ₃ CHCl ₂	2.01	CH ₃ CCl ₂ CH ₃	2.18		
CH ₂ Cl ₂	1.61	ClCH ₂ CH ₂ Cl.....	1.07	CH ₃ CH ₂ CHCl ₂	2.06		
CHCl ₃	1.05	ClCH ₂ CHCl ₂	1.15	CH ₃ CHClCH ₂ Cl.....	1.85		
CCl ₄	0.00	Cl ₂ CHCHCl ₂	1.60	ClCH ₂ CH ₂ CH ₂ Cl.....	2.24		
		ClCH ₂ CCl ₃	1.35				
		Cl ₂ CHCCl ₃	1.00				
		Cl ₃ CCCl ₃	0.00				

groups are the same for all, it would not be expected that the various halogens with such different atomic structures would give rise to the same electric moments when combined with alkyl groups. Methyl chloride, bromide, and iodide showed the most consistent change in the electric moments with the change in the halogen, and for the series of alkyl chlorides, bromides, and iodides the methyl halides seem to have a lower electric moment than the other members of the series, but above that it could hardly be said that the values are constant or that they show a trend to increase with increase in the complexity of the structure of the alkyl group. The reactivities show fairly large differences between the chloride and bromide and between the bromide and iodide, and while the differences

between two consecutive members of an alkyl series are smaller they are definite and clearly perceivable. The electric moment of monochlorobenzene is somewhat lower than that of the alkyl chlorides, but the electric moments of bromobenzene and iodobenzene are the same as that of methyl bromide and methyl iodide. From these data it must be concluded that the electric moments cannot be correlated directly with the reactivities of the halides or else that the method of determining the electric moments is not sufficiently accurate to show the small differences that are seen in reactivity measurements.

The dipole moment is a measure of electric unsymmetry, and therefore does not necessarily include the effects which may result from induced attractive or repulsive forces of either the van der Waals type or the forces induced between atoms within the molecule. Smallwood and Herzfeld (119) have found evidence of induction in the dipole moments of the ortho-substituted benzene derivatives. An inductive effect contributing to the reactivity of these substances is seen in the work of Holleman and van Haeften (46) with the chloronitrobenzenes. The carbon-hydrogen bond is a dipole, so that it may be said that in the methyl halides or the substituted methyl halides the four dipoles about the central carbon atom may exert inductive effects between the dipoles. Errera and Sherrill (27) found that the dipole moments of the heptyl halides showed a higher moment for the isomers in which the halogen atom was removed from the end position on the carbon chain, but that there was no difference for the halogen in positions along the carbon chain. On the other hand, the dipole moments of the primary, secondary, and tertiary butyl halides have been shown by Parts (93, 94) to increase, respectively. These generalizations of the electric moments are in accordance with the reactivities of these halides, but the reactivities record still smaller effects for a change in the alkyl groups of a secondary or tertiary compound. In connection with the measurements of the dipole moments of some dibromo- and bromoethoxy-pentanes and heptanes Sherrill, Smith, and Thompson (113) have recalled that when two strongly polar groups are present in the halide, the electric moments should be a resultant of the effect produced by the distortion of the molecule due to inductive forces and by rotation at the carbon-carbon bond and the two polar bonds. For the dibromopentanes and dibromoheptanes they found that there was little difference in the electric moments between all the values of the corresponding bromopentanes and bromoheptanes, but when the bromine atoms were shifted from the 1,2- to the 2,3- or 3,4-positions there was an increase in the moment. The same relationship held for the bromoethoxy-pentanes and -heptanes. Smyth and Kammerling (122) found that for the dibromides of the higher hydrocarbons the electric moments increased as the distance between the two bromine atoms in-

creased. Also, through the work of a number of investigators (see Smyth (121)), it was found that the only factor that affected the electric moments of the dichloro derivatives of methane, ethane, and propane was the position of the halogen atoms. The electric moments of the normal, iso, secondary, and tertiary butyl halides show an increase for the secondary and tertiary halides. This is considered as an induced moment which cannot be transmitted through two carbon atoms as in the case of the iso compounds. But this explanation is somewhat open to question, since the reactivities of the iso compounds show changes almost equal to the changes made by secondary compounds. Obviously, from a glance at the values of electric moments in table 21, the differences in the effects of strongly polar groups are small, and it follows that in weakly polar groups a small difference would not be observed in the electric moments. The variations in the electric moments due to effects of strongly polar groups fall much more in line with the effects observed for the reactivities of the same compounds; therefore, it would seem that reactivities record weakly polar effects more accurately than do electric moments and also tell a more complete story of the resultant effect of all the different forces. The difficulty lies in finding a mathematical interpretation of the underlying principles of reactivities.

By using the Raman effect Harkins and Bowers (39) have calculated the force constant (f) with the aid of equation 1

$$\Delta\nu = \omega_0(\nu' - \nu'') = \frac{1}{2\pi} \left(\frac{f}{\mu} \right)^{\frac{1}{2}} (\nu' - \nu'') \quad (1)$$

which is presumably the strength of the bond. They have used a number of alkyl halides and they calculated the carbon-halogen bond. A decrease in the force constant was obtained when the number of carbon atoms was increased from one to two, but from three to five carbon atoms the force constant did not change. This seemed to indicate either that the force constant actually does not change or else that it increases slightly with the number of carbon atoms, an effect that might through the reduced mass (μ) cancel the change in the force constant. The authors indicate that if the force constant is considered a constant for normal halides, the effective mass that vibrates must be located in the $-\text{CH}_2-$ group adjacent to the halogen atom, while if the force constant varies, the effective mass that vibrates must decrease. This would seem improbable. When there was a branch in the chain, the presence of it was felt only when the branching was not too far from the bromine atoms. Thus, for secondary or tertiary halides the force constant was reduced. Hukumoto (47) has calculated the dissociation energy from the absorption spectra data and found that his results were in agreement with those of Harkins and Bowers for the

Raman spectra. This work does not support the idea that the force of the carbon-halogen bond varies appreciably with the structure of the organic radical; however, it does not positively exclude the idea as impossible. Recently, Rossini (100) obtained new values for the heat of combustion of the first eight members of the paraffin hydrocarbons, C_nH_{2n-2} . From these values he showed that for the system of gaseous hydrocarbon reacting with gaseous oxygen to form gaseous carbinol, the difference in heat content for two members of the series was a constant only when the number of carbon atoms was greater than five. In order to explain this deviation from a linear function of n , he suggested that there are various kinds of C—H and C—C bonds in the normal paraffins. If the C—H bonds at the end of the chain are assumed to differ from the C—H bonds along the chain, the experimental data indicate that the methyl group at the end of the chain has a sphere of influence that includes the C—H group twice removed from it. This would indicate that the energy required to break a bond is affected by the nature of the whole molecule and that, contrary to the present idea of the strength of the bonds, they are not additive. Also Hinshelwood (45) has suggested that an electrical field rather than the thermal collision is the important factor in determining the energy of activation for these reactions, which proceed at a slower rate in solution than the collision theory would predict.

CONCLUSIONS

Investigation warrants the conclusion that reactivity of organic halogen compounds depends on the structure of the organic radical, and that reactivity is not a simple function of any one atom or group but a function of the resultant of the carbon atom holding the halogen atom and the remaining atoms or groups attached to it. The methyl halides were taken as the simplest halides and the effects of the various groups substituted in the methyl halide were examined to determine the relative influence of a grouping.

No rigid rules regulate the effect of groups, since the actual effect observed is a function of the position which a group occupies relative to the carbon-halogen bond, of the other atoms or groups attached to the carbon atom holding the halogen atom, and of the reacting substance and the solvent when their fields of force are sufficient in magnitude to exert inductive forces on the fields of force about the halide.

For aliphatic halides the reacting substance and the solvent do not in most cases appreciably affect the fields of force about the halide, and it is possible to list relatively characteristic groupings as activating or deactivating. In general, for groups substituted in place of a hydrogen atom in a methyl halide the following effects hold.

Alkyl groups decrease the reactivity. With an increase in the number of methylene groups in the alkyl group, the reactivity is consistently decreased.

When the carbon atom of the carbon-halogen bond holds a $-\text{C}=\text{C}-$,
 $\text{C}=\text{O}$, or $-\text{C}-$ grouping, the reactivity is increased.

The groupings are listed in the order of increasing ability to activate. The relative order of the  and $-\text{C}-\text{O}-\text{R}$ groupings where the R
 $\text{C}=\text{O}$

group is a methyl or ethyl group is uncertain, owing to conflicting data. The ability of these groupings to increase reactivity is greatly diminished when one carbon atom of the grouping is a carbon atom holding the halogen atom. In some cases activating groups in this position become deactivating groups in comparison to the reactivity of the methyl halide. One or more methylene groups between the carbon atom holding the halogen atom and the activating group diminishes the power of the group to increase the reactivity. The first methylene group decreases the ability to a much greater extent than do the succeeding groups.

The unusual reactivity of some tertiary compounds gives rise to the concept that the fields of force about the carbon atom holding the halogen atom and the three groups attached to it must be nearly equal to the fields of force about the halogen, or repulsive forces appear to operate.

The change in the reactivity due to a substituent in the benzene ring is difficult to correlate, because the effect of the inductive forces of the reacting substance and the solvent is apparently very great. For halides where the aromatic nucleus predominates, the solvent may even reverse the order of the reactivity.

The amines and derivatives appear to exert pronounced effects on the halides, and with these compounds the above effects may not hold.

Reactivities cannot be correlated directly with dipole moments. This would be expected in that dipole moments are a measure of electric symmetry of a compound and do not necessarily measure all the forces which may become effective. They could not measure the effects of induced fields from the reacting substance or the solvent.

Force constants calculated from spectroscopic data show evidence of effects due to some changes in structure but they do not show small effects seen in reactivity data. Recent determinations of the heats of combustion tend to support the idea that these values depend on the structure of the organic radical; thus the values for the heats of combustion bonds would not be additive.

REFERENCES

- (1) ACREE AND SHADINGER: J. Am. Chem. Soc. **39**, 226 (1917).
- (2) ADAMS AND FRENCH: J. Am. Chem. Soc. **43**, 651 (1921).
- (3) BACKER AND VON MELS: Rec. trav. chim. **49**, 177 (1930).
- (4) BADDLEY AND BENNETT: J. Chem. Soc. **1933**, 261.
- (5) BENNETT AND BERRY: J. Chem. Soc. **1927**, 1676.
- (6) BENNETT AND HACK: J. Chem. Soc. **1933**, 477.
- (7) BRADFIELD AND JONES: J. Chem. Soc. **1928**, 1006, 3073.
- (8) BRUSSOFF: Z. physik. Chem. **34**, 129 (1900).
- (9) BURKE AND DONNAN: J. Chem. Soc. **85**, 555 (1904).
- (10) CAROTHERS: J. Am. Chem. Soc. **48**, 3193 (1926).
- (11) CAROTHERS AND COFFMAN: J. Am. Chem. Soc. **54**, 4071 (1932).
- (12) CAROTHERS, COLLINS, AND KIRBY: J. Am. Chem. Soc. **55**, 789 (1933).
- (13) CAROTHERS, WILLIAMS, COLLINS, AND KIRBY: J. Am. Chem. Soc. **53**, 4203 (1931).
- (14) CLARKE: J. Chem. Soc. **97**, 416 (1910).
- (15) CHRISTIANSEN: Z. physik. Chem. **113**, 35 (1924).
- (16) CONANT AND HUSSEY: J. Am. Chem. Soc. **47**, 476 (1925).
- (17) CONANT AND KIRNER: J. Am. Chem. Soc. **46**, 233 (1924).
- (18) CONANT, KIRNER, AND HUSSEY: J. Am. Chem. Soc. **47**, 488 (1925).
- (19) COX: J. Chem. Soc. **113**, 666, 821 (1918).
- (20) COX: J. Chem. Soc. **117**, 493 (1920).
- (21) DE BARR: Am. Chem. J. **22**, 333 (1899).
- (22) DEBYE: J. Chem. Soc. **1933**, 1366.
- (23) DE MOOY: Rec. trav. chim. **35**, 19 (1916).
- (24) DRAKE AND McELVAIN: J. Am. Chem. Soc. **55**, 1155 (1933).
- (25) DRAKE AND McELVAIN: J. Am. Chem. Soc. **56**, 697 (1934).
- (26) DRUSHEL AND SIMPSON: J. Am. Chem. Soc. **40**, 674 (1918).
- (27) EBRERA AND SHERBILL: J. Am. Chem. Soc. **52**, 1993 (1930).
- (28) EULER: Ber. **39**, 2726 (1906).
- (29) EYRING AND DANIELS: J. Am. Chem. Soc. **52**, 1412 (1930).
- (30) FRANZEN AND ROSENBERG: J. prakt. Chem. **97**, 61 (1918).
- (31) FRANZEN AND ROSENBERG: J. prakt. Chem. **101**, 333 (1920).
- (32) FRENCH, McSHAN, AND JOHLER: J. Am. Chem. Soc. **56**, 1346 (1934).
- (33) GILMAN AND VAN DER WAAL: Bull. soc. chim. **45**, 344 (1929).
- (34) GOLDSWORTHY: J. Chem. Soc. **121**, 1904 (1922).
- (35) GOLDSWORTHY: J. Chem. Soc. **1926**, 1102.
- (36) GRANT AND HINSHELWOOD: J. Chem. Soc. **1933**, 258.
- (37) GRIMM, RUOFF, AND WOLFF: Z. physik. Chem. **13B**, 301 (1931).
- (38) HALFORD: J. Am. Chem. Soc. **53**, 105 (1931).
- (39) HARKINS AND BOWERS: Phys. Rev. **38**, 1845 (1931).
- (40) HARTEL AND POLÁNYI: Z. physik. Chem. **11B**, 97 (1930).
- (41) HARTEL, MEER, AND POLÁNYI: Z. physik. Chem. **19B**, 139 (1932).
- (42) HAYWOOD: J. Chem. Soc. **121**, 1904 (1922).
- (43) HECHT, CONRAD, AND BRUCKNER: Z. physik. Chem. **4**, 272 (1889).
- (44) HECHT, CONRAD, AND BRUCKNER: Z. physik. Chem. **7**, 274 (1891).
- (45) HINSHELWOOD: J. Chem. Soc. **1933**, 1351, 1357.
- (46) HOLLEMAN AND VAN HAEFTEN: Rec. trav. chim. **40**, 67 (1921).
- (47) HUKUMOTO: J. Phys. Chem. **2**, 46 (1934).
- (48) INGOLD AND PATEL: J. Ind. Chem. Soc. **7**, 95 (1930).
- (49) KHABASCH AND HANNUM: J. Am. Chem. Soc. **56**, 712 (1934).

- (50) KHARASCH AND HINKLEY: J. Am. Chem. Soc. **56**, 1212 (1934).
- (51) KHARASCH AND MAYO: J. Am. Chem. Soc. **55**, 2468 (1933).
- (52) KHARASCH, McNAB, AND MAYO: J. Am. Chem. Soc. **55**, 2521, 2531 (1933).
- (53) KINDER: Ann. **452**, 90 (1927).
- (54) KING AND McCOMBIE: J. Chem. Soc. **103**, 220 (1913).
- (55) KIRNER: J. Am. Chem. Soc. **48**, 2745 (1926).
- (56) KIRNER: J. Am. Chem. Soc. **50**, 2446 (1928).
- (57) KLAGES AND LIECKE: J. prakt. Chem. **61**, 307 (1900).
- (58) KLAGES AND STORP: J. prakt. Chem. **65**, 564 (1902).
- (59) LANGMUIR: Chem. Rev. **6**, 466 (1929).
- (60) LAPWORTH AND SHOESMITH: J. Chem. Soc. **121**, 1393 (1922).
- (61) LA MER: J. Am. Chem. Soc. **51**, 3341 (1929).
- (62) LA MER: J. Chem. Physics **1**, 289 (1933).
- (63) LA MER AND KAMMER: J. Am. Chem. Soc. **53**, 2332 (1931).
- (64) LENGFELD: Am. Chem. J. **11**, 40 (1889).
- (65) LEWIS: J. Chem. Soc. **83**, 329 (1903).
- (66) LEWIS AND HUDLESTON: J. Chem. Soc. **1932**, 1398.
- (67) LICHTY: Am. Chem. J. **17**, 27 (1895).
- (68) LOBRY DE BRUYN AND STEGER: Rec. trav. chim. **18**, 311 (1889).
- (69) LONG: J. Chem. Soc. **99**, 2164 (1911).
- (70) LUOFF: Rec. trav. chim. **20**, 292 (1901).
- (71) MADSEN: J. Chem. Soc. **103**, 965 (1913).
- (72) MEER AND POLÁNYI: Z. physik. Chem. **19B**, 164 (1932).
- (73) MENSCHUTKIN: Z. physik. Chem. **5**, 589 (1890).
- (74) MENSCHUTKIN: Z. physik. Chem. **6**, 41 (1890).
- (75) MENSCHUTKIN: Z. physik. Chem. **17**, 193 (1895).
- (76) MOELWYN-HUGHES: J. Chem. Soc. **1932**, 95.
- (77) MOELWYN-HUGHES: Chem. Rev. **10**, 241 (1932).
- (78) MOELWYN-HUGHES: J. Chem. Soc. **1933**, 1576.
- (79) MOELWYN-HUGHES AND HINSHELWOOD: J. Chem. Soc. **1932**, 230.
- (80) MOORE, SOMERVILLE, AND DERRY: J. Chem. Soc. **101**, 2459 (1901).
- (81) NATHAN AND WATSON: J. Chem. Soc. **1933**, 1248.
- (82) NEF: Ann. **309**, 126 (1899).
- (83) NORRIS AND BANTA: J. Am. Chem. Soc. **50**, 1804 (1928).
- (84) NORRIS AND BLAKE: J. Am. Chem. Soc. **50**, 1808 (1928).
- (85) NORRIS AND GREGORY: J. Am. Chem. Soc. **50**, 1813 (1928).
- (86) NORRIS AND MORTON: J. Am. Chem. Soc. **50**, 1795 (1928).
- (87) NORRISH AND SMITH: J. Chem. Soc. **1928**, 129.
- (88) OLIVIER: Rec. trav. chim. **41**, 301, 646 (1922).
- (89) OLIVIER: Rec. trav. chim. **42**, 516, 775 (1923).
- (90) OLIVIER: Rec. trav. chim. **46**, 516 (1927).
- (91) OLIVIER: Rec. trav. chim. **48**, 227 (1929).
- (92) PALOMAA AND LEIMU: Ber. **66B**, 813 (1933).
- (93) PARTS: Z. physik. Chem. **7B**, 327 (1930).
- (94) PARTS: Z. physik. Chem. **12B**, 312 (1931).
- (95) PEACOCK: J. Phys. Chem. **31**, 535 (1927).
- (96) PETRENKO: Z. physik. Chem. **116**, 313 (1925).
- (97) POLISSAR: J. Am. Chem. Soc. **54**, 3105 (1932).
- (98) PRESTON AND JONES: J. Chem. Soc. **101**, 1930 (1912).
- (99) RHINELANDER: J. Chem. Soc. **123**, 3099 (1923).
- (100) ROSSINI: Bur. Standards J. Research **13**, 21, 189 (1934).

- (101) SEGALLER: J. Chem. Soc. **103**, 1154, 1421 (1913).
- (102) SEGALLER: J. Chem. Soc. **105**, 106, 113 (1914).
- (103) SEMB AND McELVAIN: J. Am. Chem. Soc. **53**, 690 (1931).
- (104) SEMB AND McELVAIN: J. Am. Chem. Soc. **54**, 282 (1932).
- (105) SENTER: J. Chem. Soc. **91**, 460 (1907).
- (106) SENTER: J. Chem. Soc. **95**, 1827 (1909).
- (107) SENTER: J. Chem. Soc. **97**, 346 (1910).
- (108) SENTER: J. Chem. Soc. **99**, 95 (1911).
- (109) SENTER AND PORTER: J. Chem. Soc. **99**, 1049 (1911).
- (110) SENTER AND WARD: J. Chem. Soc. **101**, 2534 (1912).
- (111) SENTER AND WOOD: J. Chem. Soc. **107**, 1070 (1915).
- (112) SENTER AND WOOD: J. Chem. Soc. **109**, 681 (1916).
- (113) SHERRILL, SMITH, AND THOMPSON: J. Am. Chem. Soc. **56**, 611 (1934).
- (114) SHERODER AND ACREE: J. Chem. Soc. **105**, 2583 (1914).
- (115) SIMPSON: J. Am. Chem. Soc. **39**, 2453 (1917).
- (116) SLATOR: J. Chem. Soc. **85**, 1286 (1904).
- (117) SLATOR: J. Chem. Soc. **87**, 481 (1905).
- (118) SLATOR AND TWISS: J. Chem. Soc. **95**, 93 (1909).
- (119) SMALLWOOD AND HERZFELD: J. Am. Chem. Soc. **52**, 1919 (1930).
- (120) SMITH: J. Chem. Soc. **1933**, 1567.
- (121) SMYTH: Dielectric Constant and Molecular Structure. The Chemical Catalog Co., New York (1931).
- (122) SMYTH AND KAMMERLING: J. Am. Chem. Soc. **53**, 2988 (1930).
- (123) SOPER AND SMITH: J. Chem. Soc. **1926**, 1582.
- (124) STAUDINGER, CLAR, AND CZAKO: Ber. **44**, 1640 (1911).
- (125) STAUDINGER AND FEISST: Helv. Chim. Acta. **13**, 832 (1930).
- (126) STEWART: Chem. Rev. **6**, 403 (1929).
- (127) STRAUS: Ann. **370**, 313 (1912).
- (128) THOMAS: J. Chem. Soc. **103**, 594 (1913).
- (129) VAN DUIN: Rec. trav. chim. **41**, 402 (1922).
- (130) VAN DUIN: Rec. trav. chim. **43**, 341 (1924).
- (131) VAN DUIN: Rec. trav. chim. **45**, 345 (1926).
- (132) WARD: J. Chem. Soc. **1927**, 445, 2285.
- (133) WARD: J. Chem. Soc. **1929**, 1541.
- (134) WARD: J. Chem. Soc. **1930**, 535.
- (135) WATSON: Chem. Rev. **7**, 173 (1930).
- (136) WEDEKIND: Ann. **318**, 90 (1901).
- (137) WERNER: Ber. **39**, 1283 (1906).
- (138) WHEELER AND JOHNSON: J. Am. Chem. Soc. **24**, 680 (1902).
- (139) WILDERMAN: Z. physik. Chem. **8**, 661 (1891).
- (140) WILDERMAN: Z. physik. Chem. **9**, 12 (1892).
- (141) WISLICENUS: Ann. **212**, 239 (1882).
- (142) ZALKIND, LIFSHITZ, AND VESSELOVA: Ber. **64B**, 289 (1931).

LACHRYMATORS

KIRBY E. JACKSON AND MARGARET ARTHUR JACKSON

Department of Chemistry, Vanderbilt University, Nashville, Tennessee

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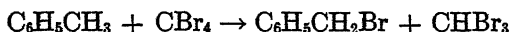
Many chemical compounds possess more or less lachrymatory properties varying in intensity from mild irritation to severe, with a flow of tears so copious as to blind the victim temporarily. Some of these compounds, like chloropicrin, are also toxic. The lachrymatory property seems to be connected with the halogen group, and all lachrymators contain one of the halogens. In general, those compounds containing iodine have the strongest lachrymatory effect; bromine compounds are less powerful and chlorine compounds still less effective (304). The comparative rarity and expense of iodine makes the use of this element impractical. Most of the lachrymators used during the World War contained bromine and some, like bromobenzyl cyanide, were extremely effective. But bromine is quite expensive as compared with chlorine, and the development of the lachrymator chloroacetophenone, which is as effective as bromobenzyl cyanide, makes it appear probable that in the future no other lachrymatory gas will be manufactured. It is an interesting fact that even as early as 1887 Prof. Bayer, in his lectures to advanced students, included a reference to the military value of lachrymators (180). When tear gas is referred to by the general public, chloroacetophenone is usually meant.

The chemical agents introduced during the World War proved very effective, as shown by the reports of the War Departments of the countries involved and the increased number of gas shells fired during the latter part of the war. Despite these facts, there is still an unholy fear of such agents on the part of the average citizen, owing to the mass of war propaganda against the use of gas and the lack of accurate information concerning same. Men fear the unknown; it is easier for them to maintain morale in the face of bullets, naked bayonets, and the sword's edge than in the presence of invisible gas; likewise a mob has less fear of the fire hose, night clubs, and bullets than of gas. There is always the uncertainty in their minds as to the effects of the gas, and more especially if there be a little smoke mixed with it, for they know not what may be behind it. The only real danger of serious injury from using non-toxic tear gas is from the possibility that members of the crowd may be trampled upon in attempts to escape.

In this paper we have studied the several lachrymatory agents which have proved effective, paying particular attention to the methods of their preparation, their physical, chemical, and physiological properties, their peace time uses, etc.

BENZYL BROMIDE, 1-BROMOTOLUENE, 1-BROMOMETHYLBENZENE, $C_6H_5CH_2Br$

Benzyl bromide has been prepared by the saturation of benzyl alcohol with hydrobromic acid (161, 302), by the action of bromine on boiling toluene (25), and by dropping bromine on toluene in the sunlight (250). If the last reaction is carried out in the dark, it has been found that a rise in temperature increases the amount of benzyl bromide, that carriers (aluminum bromide, ferric bromide, and aluminum amalgam) favor the introduction into the benzene nucleus, and that red phosphorus favors introduction into the side chain. The action of sunlight or diffused daylight, even at $25^\circ C.$, results in the formation of benzyl bromide quantitatively, but the addition of 0.5 g. of aluminum to 3 cc. of bromine causes all the bromine to enter the nucleus even in the sunlight (302). Upon treating toluene with carbon tetrabromide (155) the following reaction takes place:



Carbon tetrabromide brominates selectively the side chains of the benzene hydrocarbons instead of attacking the ring, exchanging a bromine atom for a hydrogen; bromoform is always the by-product of such bromination. Benzyl bromide is prepared by heating a mixture of benzyl benzamide with phosphorus pentabromide (49), according to the following reaction:



Holleman and Polak (150) treated toluene with bromine according to van der Laan's method (302) until all the bromine was used up; the influence of concentration and temperature on the relative amounts of benzyl bromide formed was determined as follows:

<i>Moles of toluene : 1 mole of bromine</i>		<i>Per cent of benzyl bromide formed</i>
At $25^\circ C.$	4.7	7.9
	8.0	10.6
	16.6	20.1
	25.5	36.5
At $50^\circ C.$	4.26	24.1
	8.0	42.3
	8.47	45.3
	10.47	56.2
	13.4	67.0
	20.6	82.5
	28.55	95.3

Ferric bromide, antimony bromide, or bromine do not transform benzyl bromide into bromotoluene, so the large amounts of this product obtained when the bromine concentration is large cannot be due to an autocatalysis of benzyl bromide formed as a primary product. The experiments of Cohen, Dawson, and Crosland (69), who electrolyzed concentrated hydrochloric acid under toluene, were repeated with hydrobromic acid, and it was found that, contrary to their statements, benzyl bromide was formed. This and theoretical considerations make improbable the theories of Bruner and Dluska (52) and of Bancroft (20) that bromination in the side chain is effected by bromine molecules and in the nucleus by bromine atoms. Holleman and Polak believe that free bromine molecules attack the methyl group, and that substitution in the nucleus is effected by hydrogen bromide aggregates. Hydrogen bromide decreases the volume of formation of benzyl bromide enormously. The Société Chimique des Usines du Rhône (269) received French patent 483,622 on July 26, 1917 for the preparation of benzyl bromide by the action of bromine on toluene in the presence of chlorates.

The experiments of LeBlanc and Andrich (178) on the photobromination of toluene showed the yield of benzyl bromide to be independent of the intensity of the light and constant throughout the entire portion of the spectrum investigated. The speed of the reaction decreases with decrease of wave length and is practically zero for wave lengths shorter than 300μ . Experiments on bromine in carbon tetrachloride and hexane indicate that the increased reactivity of bromine in the light is not due to the splitting-off of electrons.

A later work by Andrich and LeBlanc (5) was conducted with special reference to the influence of light of varying wave lengths on the yield of benzyl bromide. The relative proportions of benzyl bromide and bromotoluene formed during the photobromination of toluene depend upon the oxygen content of the reaction mixture; the larger the quantity of oxygen the more benzyl bromide formed. The yield of the latter substance is constant between 579μ and 325μ , and independent of small changes in bromine concentration and light intensity, but it decreases slightly with decrease in temperature. The yield of benzyl bromide was found to depend on the presence of oxygen in the reaction mixture, the yield increasing with the amount of oxygen. This had been traced to the oxidation of the hydrogen bromide, whereby bromine is regenerated. Comparative bromination experiments in the presence of hexane and ethyl acetate indicate that the free bromine molecules are photosensitive, whereas the solvated molecules are not. This relation affords an explanation of the fact that photosensitiveness of the reaction between bromine and toluene diminishes rapidly as the wave length of the incident radiation decreases. The rate

of photobromination of toluene decreases rapidly below 400μ ; the reaction is not light sensitive from 300μ to 202μ . The addition of water to the reaction mixture reduces the velocity considerably in the presence of pure oxygen, but the effect is small in the presence of air.

Benzyl bromide is a colorless liquid, with the following constants: b.p., 127°C . at 80 mm. (302), $197\text{--}198^{\circ}\text{C}$. (101), $198\text{--}199^{\circ}\text{C}$. (161), 199°C . at 749 mm. (19). Melting point, -3.9°C . (302). Density: $22^{\circ}/0^{\circ}$, 1.4380 (161); $17^{\circ}/17^{\circ}$, 1.4430; $64^{\circ}/64^{\circ}$, 1.3886 (302). It exhibits very little conductivity in liquid sulfur dioxide (306).

The following reaction velocity measurements of benzyl bromide have been made: with pyridine at 30.5°C ., 4.4 (19), at 55.6°C ., 5.118 (63); with aniline at 30.5°C ., 35 (269); with dimethylaniline at 30.5°C ., 6.34; with methylacetanilide at 30.5°C ., 0.134; with dimethyl-*o*-toluidine at

TABLE 1
Refractivity and spectral dispersion of benzyl bromide at 20°C .

BENZYL BROMIDE	n_D^t	BENZYL BROMIDE	$\frac{C}{D}$	$\frac{D}{F}$	$\frac{F}{G}$
<i>per cent</i>		<i>per cent</i>			
00.0000	1.52505	00.0000	502	1207	1017
18.8772	1.53165	18.8772	511	1245	1085
23.3439	1.53347	23.3439	519	1250	1094
33.0428	1.53669	33.0428	512	1274	1087
48.0849	1.54197	48.0849	513	1301	1117
65.3828	1.54820	65.3828	530	1319	1136
73.9944	1.55130	73.9944	538	1329	1143
78.9757	1.55295	78.9757	532	1348	1150
100.0000	1.56042	100.0000	552	1366	1180

30.5°C ., 0.235; with *p*-bromodimethylaniline at 30.5°C ., 1.93; with acetyl-piperidine at 30.5° ., 0.136 (291); with sodium sulfite at 40°C ., 5.86; at 30°C ., 18.6 (274). For the reaction of pyridine and triethylamine, respectively, with benzyl bromide in various solvents (205) the following results have been obtained: at 29°C ., in ethyl alcohol, 17.0, 39.0; in nitrobenzene, 32.3, 171.0; in benzene, 0.73, 3.70; at 45°C ., in ethyl alcohol, 56.7, 127.5; in nitrobenzene, 65.5, 369.3; in benzene, 2.26, 9.20.

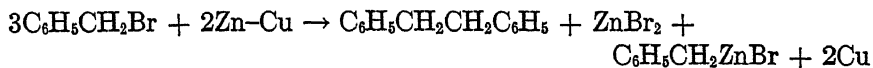
The capillary constant of benzyl bromide at 110°C . is 4.54 sq. mm.; at 156°C ., 3.81 sq. mm. (84).

Morguleva (203) determined the refractivity and spectral dispersion of benzyl bromide at 20°C ., as shown in table 1.

Alekseevskii and Alekseev (2) found benzyl bromide to be not very destructive on smooth metallic surfaces at room temperature in either dry or humid atmospheres, since the metals gradually acquire passivity.

Benzyl bromide is destroyed very slowly by water (103); the presence of small quantities of water accelerates the velocity of the reaction with organic hydroxyl groups; at 65°C. the presence of 0.44 mole of water per liter increases the velocity of the reaction 1.16 times, while the presence of 5.96 moles increases it over 2.5 times the value in absolute alcohol (131). Shoesmith and Rubli (261) carried out the hydrolysis of benzyl bromide in dilute alcohol at 25°C. and determined the value of K as 125. Benzyl bromide in water at 60°C. hydrolyzes as follows (262): at the end of 30 minutes, 22 per cent; 60 minutes, 37 per cent; 120 minutes, 59 per cent; 180 minutes, 71 per cent.

The copper-zinc couple acts vigorously on benzyl bromide with evolution of hydrogen bromide and formation of two isomers of benzylene (119), the ether-soluble modification known as α -benzylene and the ether-insoluble one as β -benzylene. In the presence of anhydrous ether the reaction is very vigorous; no hydrogen bromide is formed but instead dibenzyl, $C_6H_5CH_2CH_2C_6H_5$, as shown in the following equation:



Alcoholic ammonia reacts with benzyl bromide even in the cold to form tribenzylamine, $(C_6H_5CH_2)_3N$ (161).

By oxidation of benzyl bromide with nitric acid (density, 1.52), Flürscheim and Holmes (101) prepared, besides benzoic acid, tribromoaniline and tribromoaminobenzoic acid.

When chlorine is passed into boiling benzyl bromide in direct sunlight *p*-bromobenzyl bromide, $BrC_6H_4CHBr_2$, is obtained (92, 273).

Upon boiling benzyl bromide with dilute alcohol for two hours the respective ethers are formed (47): with methyl alcohol, benzyl methyl ether, $C_6H_5CH_2OCH_3$ b.p. 174°C.; with ethyl alcohol, benzyl ethyl ether, $C_6H_5CH_2OC_2H_5$, b.p. 189°C.; with allyl alcohol, benzyl allyl ether, $C_6H_5CH_2OC_3H_5$, a liquid with a pleasant ethereal odor, b.p. 204–205°C.

When benzyl bromide is treated with bromoform there is formed benzal bromide or benzotribromide, depending on the ratio of materials used (155).

Dufraisse and Bongrand (83) defined the threshold of concentration as the lowest concentration which the organs can detect during an exposure of 30 seconds, and took benzyl bromide as the standard with a value of unity.

Bertrand and Rosenblatt (29), experimenting upon the larvae of *Bombix neustria*, *Polychrosis botrana*, and *Eudemis botrana*, found that benzyl bromide should be placed between carbon disulfide and chloroacetone in its toxicity.

Bellay and Houdard (26), experimenting on the absorptive powers of moist garden soil, garden soil dried at 100°C., moist river sand, gravelly

sand, and vegetable humus, found that the absorptive power, which was very slight for sand, increased with the quality of vegetable humus. The action is chemical and exothermic, the soil showing a sharp change of color and an elevation of temperature, sensible to the touch. Moisture facilitates the fixation of the gas; but humus dried at 100°C. still retains 67 per cent of its absorptive power.

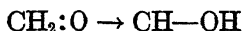
Bishopp, Roark, Parman, and Laake (33) found that all the species of flies under their observation were strongly repelled by benzyl bromide.

BROMOACETONE, BROMOPROPANONE, $\text{CH}_3\text{BrCOCH}_3$

Bromoacetone has only been prepared by the action of bromine, or a compound of the halide, on acetone. Several modified methods have been introduced but they differ only in details: by steam distilling the oily product formed by allowing bromine and acetone to stand with 10 volumes of water (270); by conducting 1.38 parts of bromine into 1 part of well-cooled acetone by means of a current of air (50, 89, 214); by introducing 1 part of bromine into 4 parts of acetone in which 1 part of marble is suspended and gradually pouring into the mixture 2.5 parts of water at 28–31°C. (248); by treating a mixture of 1 part of acetone, 1 part of glacial acetic acid, and 4 parts of water with 2.76 parts of bromine under a reflux at 70°C. (209). Lapworth (175) prepared bromoacetone by the action of bromine on acetone in the presence of various acids and bases. It has also been prepared as follows: by the action of bromine on a mixture of acetone and dilute hydrochloric acid (154); by the electrolysis of a mixture of hydrobromic acid and acetone at 35–40°C. (239); by allowing a dilute methyl alcohol solution of chloroacetone and potassium bromide to stand for several days (248); by the action of phosphorus pentabromide in petroleum ether on acetone in the cold (96); by the action of bromine and sodium bromate on a water solution of acetone in the presence of sulfuric acid (60); by the action of bromine on a dilute acetic acid solution of acetone (184).

Bromoacetone is a colorless liquid; b.p., 23.5–24.5°C. at 3.5 mm. (60), 31.4°C. at 8 mm. (248), 38–46°C. at 13 mm. (184, 209), 39.5°C. at 18 mm. (154), 40–42°C. at 13 mm. (184, 209), 48–53°C. at 25–6 mm. (50), 72–77°C. at 40 mm. (264), 136°C. (284), 136.5°C. at 725 mm. (248), 136.5°C. (7). It freezes to a colorless solid at –54°C. (7, 284). Density: 23°/23°, 1.6340 (209). It is slightly soluble in water, and easily soluble in alcohol and acetone and other organic solvents (89). It has a penetrating odor; its vapor is quickly irritating to the eyes. Bromoacetone quickly becomes violet colored in the presence of light and air (50, 89). Its vapor pressure is 1 mm. at 10°C. and 9 mm. at 20°C. (284). One cubic meter of air at 10°C. becomes saturated with 75 g. of bromoacetone in the vapor form (7).

Lapworth (175) suggests that the characteristic replacement by halogens of the α -hydrogen atom in carbonyl compounds might involve a preliminary change of the compound to its enolic form



The suggestion was based on his discovery that bromine reacts with acetone in dilute aqueous solution (to give monobromoacetone) at a rate which is proportional to the concentration of the ketone, but independent of that of the halogen; the reaction, moreover, is accelerated to a very marked extent by mineral acids (174, 176, 199). These observations led Lapworth to suggest that a slow change to the enolic form is followed by a very rapid reaction of the latter with bromine.

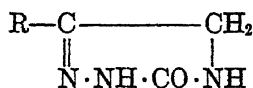


According to Sokolowsky (271) the reaction of bromoacetone with 1 mole of bromine leads to *as*-dibromoacetone, but Hughes, Watson, and Yates (154) found the mechanism of bromination of bromoacetone to be similar to that established for acetone; in water and in the absence of a catalyst bromoacetone reacts with bromine more quickly than does acetone. The autocatalytic influence of the hydrogen bromide is vastly different in the two cases: the bromination of acetone is accelerated very markedly as halogen acid accumulates in the system, but there is no appreciable autocatalysis in the case of bromoacetone. Among other products of the bromination of bromoacetone are to be found *s*-dibromoacetone, m.p. 24.1°C., b.p. 57–58°C. at 4 mm., and *as*-dibromoacetone, b.p. 38–40°C. at 7 mm.

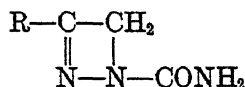
By the action of silver oxide or the alkaline carbonates on bromoacetone, an alcohol of acetone is produced, namely, acetol (acetyl carbinol), $\text{CH}_3\text{COCH}_2\text{OH}$ (89). By the action of freshly precipitated silver oxide in the presence of water, bromoacetone is converted into a liquid having a sweet taste, which appeared (88) to be an alcohol of pyruvic acid; owing to its decomposition upon dehydration it could not be obtained pure. Using the oxide of mercury on bromoacetone and treating the products of the reaction with sodium amalgam, Linnemann (188) was able to obtain only acetic acid. Acetylcarbiny acetate was prepared (51, 226) by adding bromoacetone to a warm solution of anhydrous potassium acetate in alcohol. Sokolowsky (270) obtained a crystalline compound with sodium hydrogen sulfite, and a crystalline, but unstable, compound with dry ammonia. Aqueous ammonia converts bromoacetone into basic compounds. The addition product with α -picoline melts at 196°C. (185). The cyanohydrin boils at 94.5–95.5°C. at 5.5 mm. (60). The action of monobromoacetone on ammonium sulfocyanide in an alcoholic solution forms sul-

focyanide of sulfocyanpropimine, $\text{CH}_2\text{SCN} \cdot \text{CNH} \cdot \text{HSCN} \cdot \text{CH}_3$ (214). Linnemann (185) formed the unstable addition product with bromine at 0°C ., $\text{C}_3\text{H}_6\text{O} \cdot \text{Br}_2$, along with epibromohydrin and acrolein.

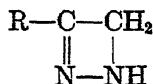
The semicarbazone of bromoacetone is easily prepared by stirring an aqueous solution of semicarbazide hydrochloride, the ketone, and sodium bicarbonate together; it melts at 135°C . It is very unstable and is decomposed by boiling water or alcohol with the formation of halogen-free compounds. Such a reaction may give rise to the formation of: (1) the six-membered ring



(2) the four-membered ring



which may pass into



by splitting off the CONH_2 group; (3) $(\text{N}:\text{CRCH}_2\text{Br})_2$, together with $(\text{NHCONH}_2)_2$; (4) $\text{HOCH}_2\text{C}(\text{:NNH}_2)\text{CH}_3$ (153).

The diethyl acetal of bromoacetone, α -bromo- β - β -diethoxypropane, a liquid with a camphor-like odor, density $0^\circ/0^\circ$, 1.1075, was prepared by Evlampiev (93) by distilling the product resulting from the action of bromoacetone and ethyl formate in a sulfuric acid solution of ethyl alcohol.

In the presence of metals, acids, or even light, bromoacetone liberates hydrogen bromide and resinifies (284), the product being a dark mass, melting above 350°C ., not reacting with phenylhydrazine or hydroxylamine but dissolving in fuming nitric acid; on dilution of this solution with water, a yellow infusible product separates which is not hydrolyzed when boiled with 50 per cent potassium hydroxide (118).

Dow (81) on April 4, 1922 received U. S. patent 1,411,422 for a lachrymatory gas composed of 40 parts of bromoacetone, 10 parts of alcohol, 10 parts of tetrachloroethylene, and 40 parts of carbon tetrachloride.

Knoll (166) found bromoacetone to be an excellent irritant with hydrocyanic acid in fumigation, but it was difficult to remove from gassed compartments.

It is impossible to remain in an atmosphere containing 30 mg. of bromoacetone per cubic meter; upon inhalation of 32 mg. per minute death ensues

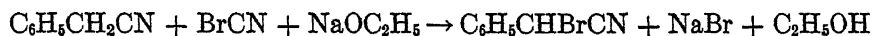
(284). The most practical method of purifying a confined space containing bromoacetone is to neutralize by spraying with an aqueous solution of sodium polysulfide and soap lye (79).

Guérin and Lormand (129) exposed several species of house plants to bromoacetone for periods of 30, 60, and 120 minutes. Most of the plants exposed for from 60 to 120 minutes in an atmosphere of 1 to 2000 parts by weight of the gas survived the toxic action. The plants lost their leaves, in consequence of plasmolysis or protoplasmic contraction (128), but new leaves grew and the plants resumed their normal vegetation.

The lachrymatory value of bromoacetone, compared with benzyl bromide taken as a standard with a value of unity, is 1.8 (83).

BROMOBENZYL CYANIDE, PHENYLBROMOACETONITRILE, α -BROMO- α -TOLUNITRILE, $C_6H_5CHBrCN$

Bromobenzyl cyanide was first prepared by Reiner (238) as the principal product from the action of bromine on benzyl cyanide at 120–130°C. Cyanogen bromide reacts with an alcoholic solution of benzyl cyanide in the presence of sodium ethoxide to form bromobenzyl cyanide (45):



Steinkopf, Mieg, and Herold (281) prepared bromobenzyl cyanide by the action of bromine vapor on phenylacetonitrile at 105°C. illuminated with a 1000-candle power Ostram-Azo lamp; Nekrasov (210) prepared it by the bromination of benzyl cyanide.

Phenylbromoacetonitrile is a yellow oil, boiling at 130°C. at 12 mm. (7), 132–134°C. at 12 mm. (281), 137–139°C. at 15 mm. (210), 231.7°C. (200), 232°C. (7). It solidifies to yellow crystals melting at 25.4°C. (210), 29°C. (7, 210, 284). Its density is 1.54 (7, 200). It is very stable, and does not appreciably decompose in air and in the presence of water at ordinary temperatures (284). It cannot be distilled even in high vacuum; it has a low vapor pressure and is thus highly persistent. It is about as toxic as chlorine, but is many times more effective as a lachrymator than any of the halogenated ketones, excepting chloroacetophenone, or aromatic halides studied. An atmosphere containing as little as 0.3 mg. per cubic meter is uninhabitable (201, 284), and 60 mg. inhaled per minute leads to death (284). It has a pleasant odor and produces a burning sensation on the mucous membrane. One cubic meter of air at 20°C. becomes saturated with 0.75 g. of bromobenzyl cyanide in the vapor form (7).

Bromobenzyl cyanide is easily converted into stilbene dicyanide by the action of an alcoholic solution of potassium cyanide; if an excess of potassium cyanide is used the product contains some dibenzylene dicyanide and a mixture of the stereoisomeric forms (57). It is converted into potassium

stilbenedicarboxylate by alcoholic potassium hydroxide and if the reaction takes place in the cold then stilbenedicarbonimide is obtained (238).

BROMOETHYL METHYL KETONE, 3-BROMOBUTANONE-2, METHYL α -BROMO-ETHYL KETONE, $\text{CH}_3\text{CHBrCOCH}_3$

With phosphorus pentabromide or bromine all ketones having hydrogen in the α -position give α -monobromoketones, as in $\text{CH}_3\text{CHBrCOCH}_3$. The formation of the latter is supposed to be preceded by enolization caused by the halogen used or arising from the dissociation of the pentahalide. Further bromination of the bromine compound introduces another bromine at the same carbon atom as the first, giving unsymmetrical dibromo derivatives as in $\text{CH}_3\text{CBr}_2\text{COC}(\text{CH}_3)_3$. With ethyl acetate, phosphorus pentabromide yields the bromide, $\text{CH}_3\text{CHBrCOCH}_3$, a liquid of a caustic odor, and reducing Fehling's solution in the cold. It boils at 35–38°C. at 12 mm.;

TABLE 2
The comparative value of the various lachrymators

LACHRYMATOR	QUANTITY NECESSARY TO PRODUCE LACHRYMATION (108)
	<i>mg. per liter</i>
Bromobenzyl cyanide.....	0.0003
Chloroacetophenone.....	0.0003
Ethyl iodoacetate.....	0.0014
Bromoacetone.....	0.0015
Xylyl bromide.....	0.0018
Benzyl bromide.....	0.0040
Chloroacetone.....	0.0180
Chloropicrin.....	0.0190

its density, 20°/20°, is 1.4380. It is converted by barium carbonate into $\text{CH}_3\text{CHOHCOCH}_3$. With 1 mole of bromine, ethyl acetate yields $\text{CH}_3\text{CHBrCOCH}_3$, while with an excess of bromine α,α -dibromoethyl methyl ketone is produced (95).

The product of the action of 1 mole of bromine or of sulfuryl bromide on ethyl methyl ketone consists of more than 67 per cent of the secondary bromo derivative, $\text{CH}_3\text{CHBrCOCH}_3$, b.p. 134–135°C. (143), 133–134°C. (303), and of nearly 33 per cent of bromomethyl ethyl ketone, $\text{CH}_2\text{BrCOC}_2\text{H}_5$, b.p. 144–145°C. (143), 145–146°C. (303). Both are nearly colorless, tear-exciting liquids which become colored in the light.

On December 15, 1926 Schering and Kahlbaum received British patent 282, 412 for the preparation of bromoethyl methyl ketone from ethylene and acetyl bromide in the presence of aluminum chloride; it boils at 55–60°C. at 15 mm. (246).

CHLOROACETONE, ACETYLMETHYL CHLORIDE, $\text{CH}_3\text{COCH}_2\text{Cl}$

Riche (240, 241) first prepared monochloroacetone by electrolyzing a mixture of hydrochloric acid and acetone; this same method has been subsequently employed by Bischoff (30), Szper (286), and Richard (239). The passage of chlorine into well-cooled, dry acetone is far a more popular method for its preparation. The following have employed this means: Glutz and Fischer (121), Kriwasin (173), Mulder (206), Barbaglia (21), Bischoff (31), Cloëz (68), and Fritsch (109, 110). Kling (162, 162a) and Mulder (206) prepared monochloroacetone by the action of hypochlorous acid on acetone. Tcherniac (287) prepared it by distilling thiocyanacetone with water in a vacuum; Linnemann (187) by distillation of monobromo(chloro)propylene with mercuric oxide and hypochlorous acid; Markownikow (193) by the action of chromic acid on chloroisopropyl alcohol; Morley and Green (204) by the oxidation of propylene chlorohydrin with chromic or nitric acid; Henry (141) by distilling a concentrated sulfuric acid solution of chloropropylene; Béhal and Detouef (24) by allowing chlorocarbamide to act on the calculated amount of an aliphatic ketone in aqueous solution.

Chloroacetone is a colorless, heavy liquid; it is slightly soluble in water but dissolves in all proportions in alcohol, ether, and chloroform. It does not form a crystalline hydrate; it volatilizes readily in water vapor. When freshly prepared it has no irritating odor, but after exposure to the air for some days it gives off irritating vapors. It is neutral to helianthin and monobasic towards phenolphthalein and Poirrier's blue (13). It is colored carmine by potassium hydroxide (206). Its boiling point is given as 117°C. (240), 117–118°C. (68), 118–120°C. (109, 110, 141, 187), 118–121°C. (30), 119°C. (21), 119°C. at 735 mm. (186), 119.7°C. (179), 120–125°C. (172). Values given for its specific gravity are 1.158 at 13°C. (68), 1.154 at 15°C. (110), 1.18 at 16°C. (187), 1.162 at 16°C. (186). Density at 17.5°/15° is 1.164 (80).

The velocity coefficient for the reaction of pyridine and chloroacetone at 55.6°C. was determined as 0.0686 (63). The dielectric constant at 19.1°C. is 29.75 ($\lambda = 60$ cm.) (80). The value for the electric moment obtained in units of 10^{18} E.S.U. is 2.17 (314). If the magnetic susceptibility, $S^M = -K \times 10^{-7}$, the value for K was determined experimentally by Pascal (221, 222, 223) as 530 as compared with 531.5, the calculated value. The absorption spectrum of the vapor of chloroacetone at various temperatures and pressures in a 200-mm. tube is described by Purvis and McClelland (234) in table 3. The vapor thus shows one very strong band, which becomes wider and stronger as the temperature and pressure increase. $N/10$ alcoholic solution showed a very large band (see figure 1).

When chloroacetophenone is conducted through a tube heated to 450°C . it forms a mixture of acetaldehyde, acetone, and crotonaldehyde (214). When it is acted upon by nitric acid (density, 1.48), oxalic acid and chloromethylnitrolic acid, $\text{CCl}(\text{NO}_2):\text{NOH}$, are formed (231).

Fritsch (110) found that when acetone is chlorinated in the usual way, the first product obtained has the boiling point ascribed to monochloroacetone, but contains about 4 per cent less of chlorine than is required for this substance, the deficiency being probably due to the presence of mesityl oxide, $(\text{CH}_3)_2\text{C}:\text{CHCOCH}_3$, formed by the action of the accumu-

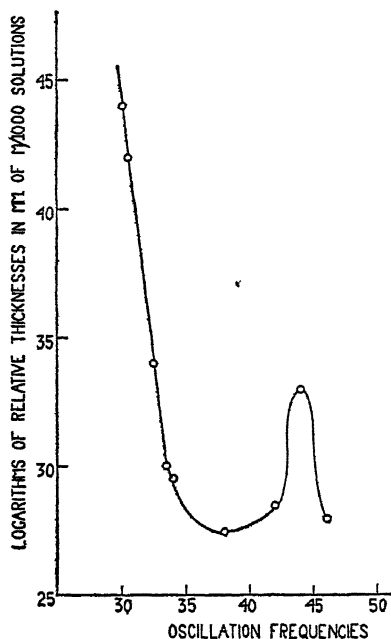


FIG. 1

lated hydrochloric acid on the excess of acetone; this conclusion is in agreement with that of Tcherniac (287). This impurity may be avoided and pure monochloroacetone formed by introducing marble into the chlorinating flask. Further chlorination of acetone, carried out in the same manner in diffused daylight, gave a product consisting of monochloroacetone mixed with both *as*-dichloroacetone, $\text{CH}_3\text{COCHCl}_2$, and *s*-dichloroacetone, $\text{CH}_2\text{ClCOCH}_2\text{Cl}$. The latter, which has not been recognized previously among the products of the direct chlorination of acetone (21, 192), is found in the fraction which boils at $167\text{--}172^{\circ}\text{C}$., and is formed to the extent of about 10 per cent of the whole. When monochloroacetone is treated with

chlorine at 100°C. in sunlight as long as the gas is absorbed, the principal product is pentachloroacetone, $\text{CHCl}_2\text{COCCl}_3$ (109).

Bromine has very little effect on chloroacetone in the cold, but at 100°C. energetic reaction takes place with the formation of chlorotribromoacetone (68). The velocity of the autocatalyzed bromination of chloroacetone reaches its minimum value when the concentration of hydrobromic acid formed is 0.002 *M* (134).

Monochloroacetone is reduced by hydrochloric acid and zinc to acetone (187).

Monochloroacetone reacts with a concentrated solution of potassium cyanide (215) to form β -methyl- β -hydroxy- γ -cyano- γ -acetobutyronitrile,

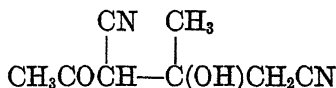


TABLE 3

Absorption spectrum of vapor of chloroacetone

TEMPERATURE	PRESSURE	RESULTS
°C.	mm.	
19	762	The rays were transmitted to $\lambda 2150$
30	806	The rays were transmitted to $\lambda 2155$
45	832	The rays were transmitted to $\lambda 2160$
60	862	The rays were transmitted to $\lambda 2180$, but they were weak between $\lambda 3080$ – $\lambda 2750$
75	891	The rays were absorbed between $\lambda 3100$ – $\lambda 2750$ and then transmitted to $\lambda 2270$
90	922	The rays were absorbed between $\lambda 3180$ – $\lambda 2580$ and then weakly transmitted to $\lambda 2340$

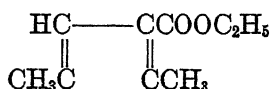
An energetic reaction sets in when chloroacetone is poured into an aqueous solution of potassium cyanide. There is formed a complicated condensation product, crystallizing from alcohol, in which it is readily soluble, in small needles, and melting at 176°C.; it has the composition, $\text{C}_{10}\text{H}_{13}\text{N}_3\text{O}$. It is tasteless and odorless, and only moderately soluble in hot water and ether. It is doubtless identical with the "cyanacetone" described by Glutz (120), but its chemical behavior indicates a high molecular weight; it cannot be readily decomposed into acetone or acetic acid and carbon dioxide, and when treated with acids and alkalis yields a complex compound, melting at 65°C. When potassium cyanide is treated with chloroacetone in alcoholic solution a dark oil, boiling above 120°C., is obtained in very small quantities, together with considerable quantities of non-volatile substances. By heating chloroacetone with a strong hydrocyanic acid-alcohol solution for twenty-four hours and evaporating the liquid, the

compound, α -hydroxy- α -chloromethylpropionitrile, $\text{CH}_3\text{C}(\text{CH}_2\text{Cl})(\text{OH})\text{CN}$, is left behind as a thin, oily liquid, which, when heated with hydrochloric acid yields α -hydroxy- α -chloromethylpropionic acid, $\text{CH}_3\text{C}(\text{CH}_2\text{Cl})(\text{OH})\text{COOH}$ (30).

Acetylcarbinol, $\text{CH}_3\text{COCH}_2\text{OH}$, is best prepared by boiling chloroacetone with anhydrous potassium or sodium formate in methyl alcohol under a reflux (209). Acetylcarbinol acetate, $\text{CH}_3\text{COOCH}_2\text{COCH}_3$, a limpid liquid having a refreshing smell and bitter taste, is prepared by treating chloroacetone with potassium acetate (51, 142, 162, 226).

By passing dry ammonia into monochloroacetone, aminoacetone, $\text{CH}_3\text{COCH}_2\text{NH}_2$, is prepared (114).

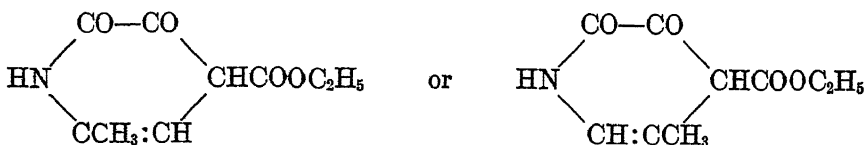
Hantzsch (135) prepared ethyl 2,5-dimethylpyrrole-3-carboxylate,



H

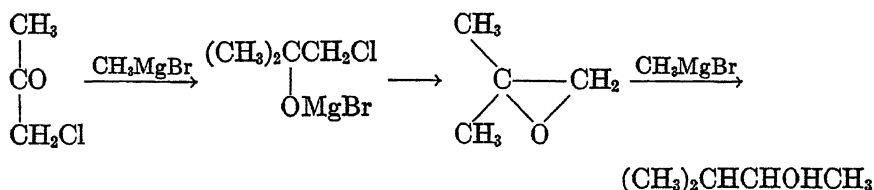
m.p. 116.7°C ., by adding concentrated ammonia to a mixture of chloroacetone and ethyl acetoacetate. Feist (99), on condensation of ethyl acetoacetate with chloroacetone and ammonia, obtained, in addition to ethyl 2,5-dimethylpyrrole-3-carboxylate, ethyl 2,4-dimethylfurfurane-3-carboxylate, which is an oil, b.p. 97°C . at 10 mm. Korschun (168) prepared methyl 2,5-dimethylpyrrole-3-carboxylate from methyl acetoacetate, chloroacetone, and dilute ammonia in the manner employed by Hantzsch for the preparation of the ethyl ester. It crystallizes from dilute alcohol, melts at 119.5°C ., and boils at 170° at 15 mm. The reaction was explained by Hantzsch as being due to the intermediate formation of ethyl β -aminocrotonate. It is not possible to prepare the ester directly from ethyl β -aminocrotonate and chloroacetone, and the reaction is better explained by Korschun by the formation of an ester of diacetylpropionic acid, which then condenses with ammonia to form the pyrrole derivative.

When ammonia is passed into an ethereal solution of ethyl oxalate and chloroacetone, condensation ensues with the formation of oxamide and ethyl oxymethylpyridonecarboxylate (99):



Methylmagnesium bromide in ethereal solution reacts with chloroacetone giving the compound, $\text{CH}_2\text{ClC}(\text{CH}_3)_2\text{OMgBr}$, which, on heating in ethereal

solution, forms magnesium chlorobromide and isobutylene oxide; the latter, when again treated with the organomagnesium halide, forms methylisopropylcarbinol (146):



Fourneau and Tiffeneau (104) obtained the chlorohydrin of methylethylglycol, $\text{C}_2\text{H}_5\text{C}(\text{CH}_3)\text{OHCH}_2\text{Cl}$, b.p. $152\text{--}153^\circ\text{C}$., density 1.068 at 0°C ., and the alcohol, $(\text{C}_2\text{H}_5)(\text{CH}_3)\text{CHCHOHC}_2\text{H}_5$, b.p. $149\text{--}151^\circ\text{C}$., density 0.8518 at 0°C ., as the result of the action of methylmagnesium bromide on chloroacetone.

By the interaction of chloroacetone and dimagnesiumdibromoacetylene, there is obtained the product, $\text{CH}_3\text{C}(\text{CH}_2\text{Cl})(\text{OH})\text{C}\equiv\text{CC}(\text{OH})(\text{CH}_2\text{Cl})\text{CH}_3$, an oil (density: $0^\circ/4^\circ$, 1.277; $20^\circ/4^\circ$, 1.257); it does not distil at 6 mm. and does not crystallize (313).

When phenylmagnesium bromide in ether reacts on chloroacetone, the reaction mixture being kept cold, there is formed methylchlorostyrolene, $\text{C}_6\text{H}_5(\text{CH}_3)\text{C}:\text{CHCl}$, diphenyl, $\text{C}_6\text{H}_5\text{C}_6\text{H}_5$, methylstilbene, $\text{C}_6\text{H}_5\text{C}(\text{CH}_3):\text{CHC}_6\text{H}_5$, and the alcohol, $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CHOHC}_6\text{H}_5$ (296). After the organomagnesium halide is allowed to react on chloroacetone, the reaction mixture is cooled to room temperature and the complex magnesium compound heated to $130\text{--}140^\circ\text{C}$.; upon decomposing the resulting product with dilute sulfuric acid phenylacetone, $\text{C}_6\text{H}_5\text{CH}_2\text{COCH}_3$, is formed (294, 297).

The action of chloroacetone on phenylmagnesium bromide yields the chlorohydrin $\text{HOC}(\text{C}_6\text{H}_5)(\text{CH}_3)\text{CH}_2\text{Cl}$; on methylmagnesium iodide the chlorohydrin, $\text{HOC}(\text{CH}_3)_2\text{CH}_2\text{Cl}$; on ethylmagnesium bromide the chlorohydrin, $\text{HOC}(\text{CH}_3)(\text{C}_2\text{H}_5)\text{CH}_2\text{Cl}$ (293). These results are regarded as supporting Krassusky's (171) conclusion that when hypochlorous acid combines with ethylenic hydrocarbons the hydroxyl group always attaches itself to the carbon atom combined with the smallest number of hydrogen atoms.

Hexamethylenetetramine forms with chloroacetone a crystalline additive product, which is obtained as lustrous needles melting at 122°C . (191).

By the action of trimethylamine on monochloroacetone, trimethylacetonylammonium chloride, $\text{CH}_3\text{COCH}_2\text{N}(\text{CH}_3)_3\text{Cl}$, is produced as a crystalline, very deliquescent mass (111, 213, 247).

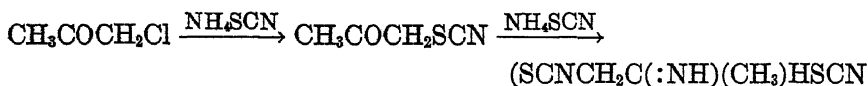
Dimethylaminoacetone, $\text{N}(\text{CH}_3)_2\text{CH}_2\text{COCH}_3$, is prepared by adding

chloroacetone to an aqueous 30 per cent solution of dimethylamine. It is a colorless oil, miscible with water, alcohol, and ether in all proportions, and becomes brown on exposure to air; it boils at 123°C. (282).

Upon heating chloroacetone, ethyl orthoformate, alcohol, and a drop or two of concentrated sulfuric acid there is formed monochloroacetone ethyl-acetal, $\text{ClCH}_2\text{C}(\text{CH}_3)(\text{OC}_2\text{H}_5)_2$ (a colorless liquid with a pleasant odor, b.p. 162–163°C., b.p. 57°C. at 12 mm., density 14°/0°, 1.0002 (8)), and α -chloro- β , β -diethoxypropane, b.p. 52–53°C. at 14 mm. (93).

Scholl and Matthaopoulos (248) prepared chloroacetoxime, $\text{CH}_2\text{ClC}(\text{CH}_3):\text{NOH}$, by treating chloroacetone with less than the theoretical amount of hydroxylamine hydrochloride and sodium carbonate; the substance boils at 71.2°C. at 9 mm., 84.5°C. at 21 mm., 98°C. at 45 mm., 171°C. at 727 mm. Methylglyoxime (acetoximic acid) $\text{CH}(:\text{NOH})-\text{C}(:\text{NOH})\text{CH}_3$, m.p. 156°C. is also formed at the same time, but it is the only product if about three times the theoretical amount of hydroxylamine is used (136).

By stirring a mixture of chloroacetone and a solution of sodium thiocyanate, Tcherniac (288) obtained thiocyanacetate, $\text{CH}_3\text{COCH}_2\text{SCN}$. This was first obtained by the action of chloroacetone on barium thiocyanate in alcoholic solution (139), but later it was found that the reaction takes place in the absence of alcohol when the crystalline barium salt is intimately mixed with the ketone. Tcherniac and Norton (289, 290) found that when ammonium thiocyanate acts on chloroacetone in alcohol solution, thiocyanacetone is formed, but that it reacts with the excess of the ammonium salt to produce the thiocyanate of a new base which they named thiocyanopropimine. These changes may be expressed thus:



When chloroacetone and phenylhydrazine, both dissolved in absolute alcohol, were mixed and allowed to stand in a freezing mixture, a yellow crystalline mass separated which melted at 162.5°C. and which proved to be the phenylhydrazone of phenylhydrazinoacetate, $\text{NHC}_6\text{H}_5\text{NHCH}_2-\text{C}(\text{CH}_3):\text{NNHC}_6\text{H}_5$ (27, 35).

In the presence of metals, acids, or even light, monochloroacetone resinifies, the product being a dark mass, melting above 350°C., which liberates hydrogen chloride in air. It does not react with phenylhydrazine, hydroxylamine, or oleum. It dissolves in fuming nitric acid, and on dilution with water a yellow infusible product separates. Boiling with 50 per cent potassium hydroxide does not hydrolyze the product (118).

1,2,2-Tri(hydroxyphenyl)propane, $\text{CH}_3\text{C}(\text{C}_6\text{H}_4\text{OH})_2\text{CH}_2\text{C}_6\text{H}_4\text{OH}$ is prepared by heating chloroacetone with 3 moles of phenol and fuming hy-

drochloric acid. It decomposes at 175°C. 1,2,2-Tri(dihydroxyphenyl)-propane, $\text{CH}_3\text{C}[\text{C}_6\text{H}_3(\text{OH})_2]_2\text{CH}_2[\text{C}_6\text{H}_4(\text{OH})_2]$, prepared in a similar manner from resorcinol, gives a colorless or faintly red colored substance, m.p. 180°C. (189).

Lecat (179), using 71.5 per cent toluene (b.p., 110.75°C.) and chloroacetone (b.p., 119.7°C.), formed an azeotrope boiling at 109.2°C.

Slator and Twiss (267) found chloroacetone to react rapidly with sodium thiosulfate, the velocity constant being 0.134 at 15°C. and 0.375 at 25°C.

Chloroacetone and diazomethane react to form chloroisobutylene oxide,



O

b.p. 124°C., and a mixture of higher oxides (10).

Chloroacetone 4-*m*-nitrophenylsemicarbazone, $\text{CH}_2\text{ClC}(\text{CH}_3)\text{C}=\text{NNHCONHC}_6\text{H}_4\text{NO}_2$, prepared by mixing chloroacetone with *m*-nitrophenylsemicarbazide hydrochloride, forms pale yellow needles melting to a semi-solid at 223°C. and to a dark brown liquid at 238°C. (309).

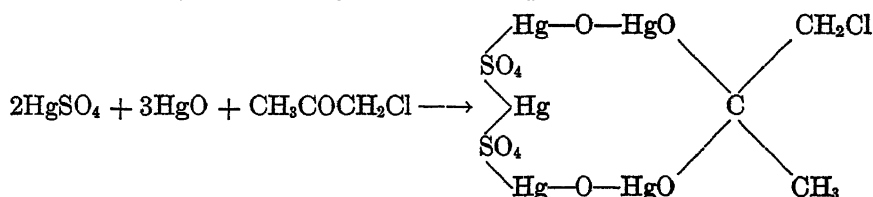
Chloroacetone semicarbazone, m.p. about 150°C., is prepared by stirring aqueous semicarbazide hydrochloride, chloroacetone, and sodium bicarbonate together (153).

The *p*-bromophenyl-4-semicarbazone of chloroacetone is prepared by heating an alcoholic solution of the semicarbazide with an excess of the ketone; upon cooling beautiful crystals separate, which decompose upon melting at 182°C. (308).

Monochloroacetone is not as easily reduced as the dichloroacetone, since it tends to inhibit fermentation, yet a 25 per cent yield of monochloroisopropyl alcohol, $\text{CH}_3\text{CH}(\text{OH})\text{CH}_2\text{Cl}$, is obtained when an alcoholic solution of monochloroacetone is added over a period of several hours to a mixture of pressed beer yeast and starch or cane sugar dissolved in water and allowed to stand for some hours at 35°C. (257).

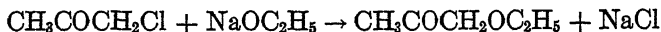
An aqueous solution of benzenediazonium chloride at 0°C. in the presence of sodium acetate gives with chloroacetone a reddish yellow precipitate, probably the azo derivative, $\text{CH}_3\text{COCHClN}:\text{NC}_6\text{H}_5$, which is rapidly transformed into the phenylhydrazone of pyruvyl chloride, $\text{CH}_3\text{COCCHCl}:\text{NNHC}_6\text{H}_5$, melting at 136–137°C. (97).

When monochloroacetone reacts with a solution of mercuric sulfate and mercuric oxide, the following reaction takes place:



The resulting product is an insoluble solid which dissolves in hydrochloric acid and decomposes explosively when heated to about 133°C. (78).

Sodium ethylate and chloroacetone react very rapidly (138), so much



so that the equilibrium constant has not been determined, but when equivalent quantities of sodium ethylate and chloroacetone of concentration 0.05 *N* were used at 0°C. the course of the reaction could be followed graphically from the following data:

TIME	CLEAVAGE	1000 <i>K</i>
<i>minutes</i>	<i>per cent</i>	
1	31.4	965
2	40.9	705
6	52.4	379
15	60.7	184

This is further illustrated in figure 2.

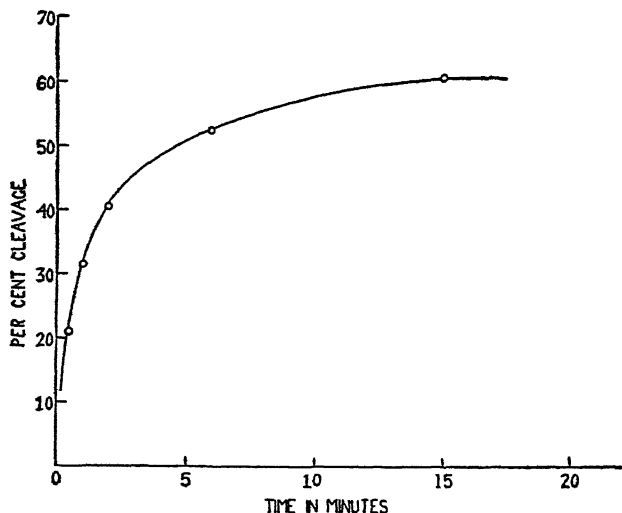


FIG. 2

The condensation of chloroacetone with 2,4-dinitrophenylhydrazine first gives chloroacetone 2,4-dinitrophenylhydrazone, $(\text{NO}_2)_2\text{C}_6\text{H}_3\text{NHN}:\text{C}(\text{CH}_3)\text{CH}_2\text{Cl}$, yellow needles, m.p. 124–125.5°C. Prolonged boiling in alcoholic solution converts it into the corresponding osazone, $(\text{NO}_2)_2\text{C}_6\text{H}_3\text{NHN}:\text{CHC}(\text{CH}_3):\text{NNHC}_6\text{H}_3(\text{NO}_2)_2$, dark red crystals, m.p. 298°C. (53).

Two cases have been reported where small colorless bottles containing monochloroacetone have exploded. The contents had polymerized to a black rubber-like substance without lachrymatory properties and smelling strongly of hydrogen chloride but free from chlorine (3, 94).

Dufraisse and Bongrand (83) compared the activity of chloroacetone with that of benzyl bromide by determining the concentration in atmospheres necessary to produce the same lachrymogenic effect. The power of the substance studied will be inversely as its concentration thus determined. The "concentration de seuil" of chloroacetone was determined as 0.125. Bertrand (28), commenting on the work of Dufraisse and Bongrand, shows that the minimum concentration of a lachrymatory substance which is perceptible depends not only on the observer, but also on the duration of the exposure. Thus chloropicrin acts suddenly, and but slowly increases its intensity on prolonged contact; monochloroacetone acts with progressively increasing intensity. The different actions of these agents is ascribed to their varying solubility in the aqueous liquids of the eye. Thus the method of Dufraisse and Bongrand does not give a correct comparison between different lachrymatory substances.

Bertrand and Rosenblatt (29) performed experiments on the larvae of *Bombix neustria*, *Polychrosis botrana*, and *Eudemis botrana*. The insects were subjected to the action of measured amounts of air and poisonous vapor from several chemicals; chloroacetone was found to be much more effective than ether, chloroform, carbon disulfide, or carbon tetrachloride.

CHLOROACETOPHENONE, PHENACYL CHLORIDE, BENZOYL CARBINOL CHLORIDE,
 $C_6H_5COCH_2Cl$

Chloroacetophenone was first prepared by Graebe (124) in 1871 by passing a stream of chlorine into boiling acetophenone; since that time Staedel (276), Dyckerhoff (86), Gautier (117), and Korner and Scholl (169) have prepared the chlorinated acetophenone in a similar manner. By dissolving chloroacetyl chloride in benzene and adding aluminum chloride, Friedel and Crafts (106) and Tutin (300) prepared chloroacetophenone. It is also prepared by the oxidation of diphenacyltelluride dichloride with potassium permanganate (243); by the action of monochlorourea on an aqueous solution of acetophenone (24); by treating an ethereal solution of aromatic acyl chlorides with diazomethane (67, 280); by the electrolysis of hydrochloric acid in an aqueous solution of acetophenone and acetic acid at 5.6–6.5 volts and 0.6 ampere per square decimeter (286).

Chloroacetophenone crystallizes from dilute alcohol in rhombic plates (107) whose axial ratios ($a:b:c$), were determined by Aminoff (4) as 0.9957:1:0.4270 and by Staedel (276) as 0.9957:1:0.2135. Its melting point has been given as 41°C. (124), 55–59°C. (284), 56°C. (18, 106),

58.5°C. (7), 58–59°C. (67, 243, 276), 59°C. (300); its boiling point as 113°C. at 18 mm. (16), 139–141°C. at 14 mm. (67), 241–242°C. (106), 244–245°C. (276), 244.5°C. (7), 245°C. (284), 246°C. (124). Density: 15°/4°, 1.3240 (4, 117); 16.6°/4°, 1.2016; 20°/4°, 1.198 (16). It is practically insoluble in water (about 1 g. per liter at room temperature) (284), but is easily soluble in alcohol, ether, and benzene. It has an agreeable aromatic odor but its vapor acts very strongly on the eyes (117, 124, 276). Its vapor pressure is 0.0028 at 0°C. (284, 304). One cubic meter of air at 0°C. is saturated with 30 mg. and at 20°C. with 105 mg. of chloroacetophenone (7).

The following reaction velocity measurements of chloroacetophenone have been made: with sodium thiosulfate in dilute alcohol at 15°C., 0.65 (267); with pyridine in absolute alcohol at 55.6°C., 0.1339 (63); with pyridine in 90 per cent alcohol at 30.5°C., 0.11 (18); with 1 mole of acetone solution of potassium iodide with 5 moles of the chloroacetophenone at 0°C. is 22.4 (72). With equimolecular quantities of chloroacetophenone and aniline in absolute alcohol at 40°C. it was found that no reaction occurred, but with 2 moles of the chloroacetophenone and 5 moles of the aniline the reaction was rapid, the value of $k \times 10$ being 0.67 (194).

Exposed to light, chloroacetophenone rapidly turns green. Upon oxidation it yields benzoic acid entirely free of chlorine, which proves conclusively that the chlorine is contained in the methyl group. It is unchanged by boiling water, but on heating with water in sealed tubes hydrogen chloride is formed and also a solid of very high boiling point (124).

If, during the preparation of chloroacetophenone, more chlorine is passed into the vapor of acetophenone than is necessary for taking up 1 atom of chlorine, the product obtained is essentially different from the ordinary one. On fractional distillation a liquid passes over at 250–255°C., which consists chiefly of the dichloride. By the continued action of chlorine, a dark, thick mass is obtained, which, on distillation, yields a small quantity of a liquid which consists chiefly of benzoyl chloride. That portion with highest boiling point contains products poorer in chlorine. Analysis gave numbers pointing to the formula $C_{16}H_{11}O_2Cl$. Possibly this substance was formed in a similar way to the chlorides obtained by Staedel (275) by the removal of 1 mole of hydrogen chloride from 2 moles of chloroacetophenone. At a temperature above 360°C. a substance passed over which solidified in amorphous masses on cooling, and emitted a smell of oil of bitter almonds. The occurrence of benzoic acid was also noted. The formation of benzoyl chloride and benzoic acid may be explained in two ways: (1) It may be supposed that chlorine was gradually substituted for the hydrogen atoms of the methyl group, and finally split off, the $-CCl_3$ residue taking its place, and forming benzoyl chloride. Carbon tetrachloride must have been formed at the same time, though it could not be

detected. In the preparation of chloroacetophenone, water is always formed, and it may possibly convert the benzoyl chloride partly into benzoic acid. (2) The water formed from the acetophenone may, in the presence of the chlorine, exercise an oxidizing influence, so that from a small part of the acetophenone benzaldehyde may be first formed, which may then be partly converted, by further oxidation, into benzoic acid, while another part passes, under the influence of the chlorine, into benzoyl chloride (86).

When an ethereal solution of chloroacetophenone is treated with ammonia two isomeric substances, α - and β -chlorodiphenacyl, are formed; one is readily soluble in alcohol and ether and crystallizes in needles melting at $117^{\circ}\text{C}.$, while the other is much less soluble and forms prisms melting at 154 – $155^{\circ}\text{C}.$ (277, 279). Chlorodiphenacyls were also prepared by the action of sodium ethoxide on chloroacetophenone in absolute alcohol (220). It was later found (219) that the mother liquor after the crystallization of α - and β -chlorodiphenacyls contained a small quantity of a compound, $\text{C}_{16}\text{H}_{13}\text{O}_2$, which crystallized from alcohol in white needles melting at $189^{\circ}\text{C}.$, and which is an isomer of the chlorodiphenacyls but yields no diphenacyl on reduction.

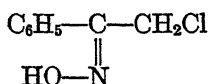
When chloroacetophenone is heated for 1.5 hours at $100^{\circ}\text{C}.$ in a sealed tube with an excess of alcoholic ammonia, there is obtained a dark bluish green substance which, after purification, crystallizes from xylene in large, colorless plates, melting at $194^{\circ}\text{C}.$; it is identified as 2,5-diphenylpyrazine. The original alcoholic filtrate, after further treatment, is found to contain colorless needles, melting at about $189^{\circ}\text{C}.$ and identified as 2,6-diphenylpyrazine monochloride, which yields 2,6-diphenylpyrazine, colorless needles, melting at $90^{\circ}\text{C}.$ (300). When chloroacetophenone is heated with dilute ammonia in excess of air 2,5-diphenylpyrazine is formed (276, 278).

Ammonia and chloroacetophenone readily act on each other, even in the cold, more quickly on heating, and yield several products: one of them, with the composition $\text{C}_8\text{H}_7\text{N}$, crystallizes from hot benzene or glacial acetic acid in glistening, serrated plates, melting at 194 – $195^{\circ}\text{C}.$ and subliming in pearly plates; another substance was probably identical with Graebe's (125) benzoylcarbinol, $\text{C}_6\text{H}_5\text{COCH}_2\text{OH}$ (278).

The view which has been several times put forward that α -halogen ketones containing the grouping $-\text{CO}-\text{CHCl}$ are converted by hydroxylamine directly into glyoximes without the formation of intermediate products was shown by Scholl and Mathaiopoulos (248) to be erroneous in the case of aliphatic compounds, while under suitable conditions they yield α -halogen ketoximes. Korten and Scholl (169) find that analogous compounds can be obtained in the aromatic series if the hydroxylamine be made to act in the presence of a mineral acid. In this way, chloroaceto-

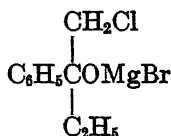
phenone yields aromatic α -halogen ketoximes which are readily crystallizable compounds belonging to the *syn*-phenyl series. When the hydroxylamine is employed in alkaline solution, the glyoxime obtained is accompanied by a small proportion of the *anti*-phenyl ketoxime. The halogen of these α -halogen ketoximes readily reacts with alkalis and ammonia, in the latter case yielding tertiary amines which, under the action of alcoholic hydrochloric acid, are partially deoximated and transformed into paroxazine derivatives.

Syn-phenyl chloromethyl ketoxime,



obtained by the interaction of chloroacetophenone (1 mole) and hydroxylamine hydrochloride (3 moles) in dilute methyl alcohol at ordinary temperature, separates from carbon disulfide in crystals melting at 88.5–89°C. Its vapors are very painful to the eyes; when placed on the skin in either the solid or the dissolved state it produces a very persistent burning sensation (169).

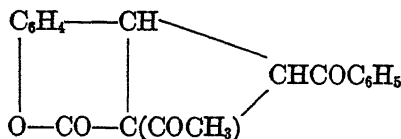
Chloroacetophenone yields on action of ethylmagnesium bromide in ether a complex magnesium compound,



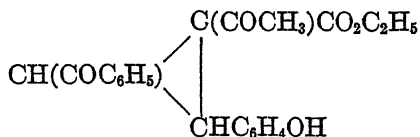
which, upon heating, changes to ethyl benzyl ketone, $\text{C}_6\text{H}_5\text{CH}_2\text{COC}_2\text{H}_5$, b.p. 221–223°C. Its semicarbazone melts at 146°C. (297).

Upon boiling molecular quantities of chloroacetophenone and potassium sulfocyanide under a reflux for a short time, an ether is obtained which crystallizes from alcohol, ether, and chloroform in long needles having the composition expressed by the formula, $\text{C}_6\text{H}_5\text{COCH}_2\text{SCN}$; it melts at 72–73°C. (85).

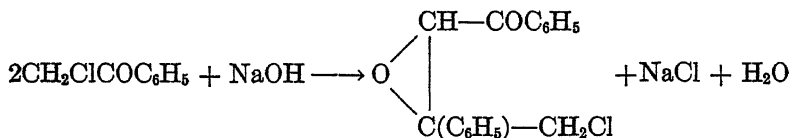
When 3-acetylcoumarin and chloroacetophenone are mixed in cold alcohol and treated with sodium ethylate solution, two products are obtained, the chief one being 3-acetyl-3,4-phenacylidene coumarin,



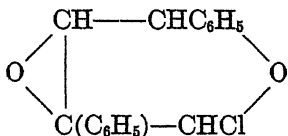
which crystallizes in silky needles, m.p. 184°C.; the other compound, which is the more soluble in alcohol, is ethyl α -acetyl- α,β -phenacylidene-coumarate,



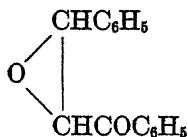
which crystallizes in brilliant quadratic prisms, m.p. 117°C. The condensation must proceed rapidly, as chloroacetophenone gives rise to 2-chloro-3,4-oxido-3,5-diphenyltetrahydrofuran when left with sodium alkyl oxides alone (311). The course of the reaction whereby chloroacetophenone and alcoholic sodium ethoxide yield oxidotetrahydrofuran is, in its first stage, probably analogous to those described by Darzen (75) and by Claisen (62), in which ketones or aldehydes condense with esters of halogenated fatty acids in the presence of sodium ethoxide or of sodamide to form esters of substituted glycidic acids:



The intermediate product then does not yield a four-membered ring by loss of hydrogen chloride, but is converted into a furane derivative



The two suppositions in this explanation are supported by experimental evidence. With regard to the formation of the oxido groups Widman and Almström (312) find that chloroacetophenone and benzaldehyde in the presence of alcoholic sodium ethoxide, in accordance with Darzen's statement that esters of halogenated fatty acids condense preferentially with aldehydes rather than with ketones, yield not a trace of a furane derivative, but a substance (m.p. 89–90°C.) which proves to be α -benzoyl- β -phenyl-ethylene oxide



The second supposition that a ketone containing a halogen atom in the γ -position to the carbonyl group is capable of yielding a furane derivative, is supported by the behavior of a substance described by Perkin (225) as phenyl bromopropyl ketone, $\text{C}_6\text{H}_5\text{COCH}_2\text{CH}_2\text{CH}_2\text{Br}$. This substance, however, does not exhibit the properties of a ketone, and is most probably 2-bromo-5-phenyltetrahydrofuran.

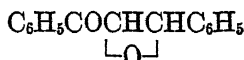
Upon distilling a mixture of chloroacetophenone and phosphorus pentachloride at $225\text{--}231^\circ\text{C}$., α,β -dichlorostyrol, $\text{C}_6\text{H}_5\text{CCl}:\text{CHCl}$, a colorless, oily liquid, boiling at 221°C . and possessing a pleasant odor, is formed (85).

By saturating a cold glacial acetic acid solution of chloroacetophenone and *m*-nitrobenzaldehyde with hydrogen chloride and allowing to stand for twenty-four hours, then condensing *in vacuo*, there is obtained phenyl α,β -dichloro- β -(*m*-nitrophenyl)ethyl ketone, $\text{C}_6\text{H}_5\text{COCHClCHClC}_6\text{H}_4\text{NO}_2$, colorless needles melting at 148°C . (34).

Chloroacetophenone and hexamethylenetetramine form a salt-like additive product melting at 145°C . On treatment for three days with hydrochloric acid and alcohol it gives the hydrochloride of aminoacetophenone, m.p. $196\text{--}197^\circ\text{C}$. (191).

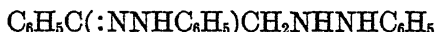
Knöpfer (165) prepared the chloroacetophenone semicarbazone, $\text{C}_6\text{H}_5\text{ON}_3\text{Cl}$, in the form of white crystals melting at 137°C .

When a mixture of benzaldehyde and chloroacetophenone in cold alcohol is treated with sodium ethoxide, benzoylphenyloxidoethane,

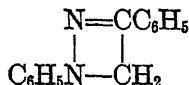


is formed, plates, m.p. $89\text{--}90^\circ\text{C}$. (310).

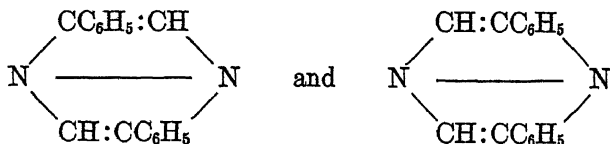
The reaction between chloroacetophenone and phenylhydrazines may take the following course (152): (1) with the formation of a hydrazone; (2) with the formation of compounds of the type



(3) with the formation of compounds of the type



(4) the reaction may take a course similar to the reaction between chloroacetophenone and ammonia, giving 2,5- and 2,6-diphenylpyrazines (112, 113, 278, 300)



By the action of an alcoholic solution of potassium acetate, chloroacetophenone is converted into the acetate of acetylbenzene alcohol, $C_6H_5COCH_2OCOCH_3$ which melts at $44^\circ C.$ and boils at $270^\circ C.$ On cooling, or by crystallization from alcohol, it is obtained in large rhombic plates, insoluble in water, easily soluble in alcohol and ether; it has a pleasant aromatic odor. The alcohol may be obtained directly from chloroacetophenone by heating with a solution of sodium carbonate or with plumbic hydrate and water, and from the acetate with alcoholic potash solution; in both cases, however, it is mixed with considerable quantities of by-products. In the impure state in which it has hitherto been obtained, it forms a pleasant-smelling body insoluble in water (124).

When chloroacetophenone is heated with benzene and aluminum chloride to $100^\circ C.$ there is no reaction, but when it is heated with toluene and aluminum chloride to $111^\circ C.$ (the boiling point of toluene) there is produced methyldeoxybenzoin, $C_6H_5COCH_2C_6H_4CH_3$, small crystals, m.p. $84-85^\circ C.$ (70).

Chloroacetophenone does not react with sodium bisulfite (117).

Dean and Berchet (76) found that chloroacetophenone reacts with sodium and anhydrous ammonia in the ratio of 1 mole of halide to 2.2 moles of sodium. A reddish oil was obtained which was nitrogen- and halogen-free. There was also separated 0.4 g. of a colorless solid, m.p. $73-74^\circ C.$, which was unidentified.

Chloroacetophenone is a most effective substance to be used as a warning agent for inflammable and poisonous gases: 0.021 and 0.0083 part per million is all that is required for nasal and eye irritation (159). Hanslian (133) found that lachrymation begins with 0.5 mg. per cubic meter, nasal irritation starts at 1 mg. per cubic meter, irritation of the skin about the face and throat (especially in mouth breathing) occurs at about 2 mg. per cubic meter. It is unbearable to remain in an atmosphere of 5 mg. per cubic meter for more than a few seconds at a time and a concentration of 100 mg. per cubic meter causes burns. Hanzlik and Tarr (137) found chloroacetophenone to be a mild skin irritant as indicated by simple hyperemia without vesication, mild urticarial rash, moderate swelling and edema, and very little or no necrosis.

For the quantitative determination of chloroacetophenone, Chrzasczewska and Chwalinski (59) suggest the use of sodium sulfide.

On December 15, 1925, U. S. patent 1,565,899 was issued to Bradner for a cartridge for the effective dissemination of chloroacetophenone (43) and on September 21, 1926, U. S. patent 1,600,223 was issued to Goss for a cartridge for disseminating chloroacetophenone (122); U. S. patent 16,841 for a means of volatilizing chloroacetophenone (44) was reissued January 3, 1928.

The use of a mixture of chloroacetophenone and hydrocyanic acid in ship fumigation brought out the fact that chloroacetophenone remained long after the hydrocyanic acid and that the two gases tended to form pockets rather than a uniform mixture (6).

Chloroacetophenone has been found to be an effective larvicide for the screwworm and all species of flies under observation (33).

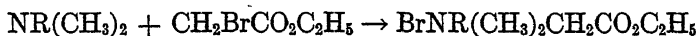
ETHYL BROMOACETATE, $\text{CH}_3\text{BrCOOC}_2\text{H}_5$

Ethyl bromoacetate was first prepared by Perkin and Duppa (228, 229) by heating bromoacetic acid and alcohol in a sealed tube for an hour at 100°C .; from bromoacetic acid anhydride and alcohol (116); by the action of monobromoacetyl bromide and alcohol (207); by heating red phosphorus and bromine with glacial acetic acid on the water bath for six hours and pouring the product into excess alcohol (15); by treating bromoacetylchloride in alcohol with red phosphorus (115); from the action of phosphorus pentabromide on ethyl glycolate (140); by the action of bromine on sodium ethylate (256); by the action of cyanogen bromide on diethylaminoacetonitrile (46); by passing gaseous hydrogen bromide into a chloroform solution of ethyl diazoacetate (73). Slimmer (268) upon heating dibromophenoxyethylene for seven hours at 110°C . with alcoholic potash obtained ethyl bromoacetate and not phenoxybromoacetylene as stated by Sabaneff and Dworkowitsch (244). Imbert (156) on October 4, 1906 received German patent 212,592 for the preparation of ethyl bromoacetate from dibromovinyl ether and alcohol, in the absence of water, but in the presence of catalyzers such as aluminum chloride at the ordinary temperature, heating being required in the presence of water. Henry (144, 145) obtained the ester after the method described by DeMole (77), who treated the monoacetin of ethylene glycol with hydrobromic acid.

Ethyl bromoacetate is a not unpleasant smelling, colorless, very mobile liquid of sweetish-caustic taste, which violently attacks the mucous membrane, particularly the eyes. Its boiling point has been given as 122 – 125°C . at 738 mm. (301), 159°C . (11, 15, 115, 228, 305), 159 – 160°C . (140, 245), 161 – 163°C . (77), 162 – 163°C . (144, 145), 168.7°C . (corrected) (227). It solidifies in freezing mixture of carbon dioxide and ether to colorless needles, melting at -13.8°C . (144, 145). Density: $4^\circ/4^\circ$, 1.5282; $10^\circ/10^\circ$, 1.5192; $15^\circ/15^\circ$, 1.5123; $20^\circ/20^\circ$, 1.5059; $25^\circ/25^\circ$, 1.5002. Refractive index determinations: density $13^\circ/4^\circ$, 1.51414, η $13^\circ/\alpha$, 1.45160; η $13^\circ/\text{D}$, 1.45420; η $13^\circ/\gamma$, 1.46631. The magnetic rotation twice determined (72 readings) gave: t , 16.6°C .; specific rotation, 1.2386; molecular rotation, 7.609 (227). If the magnetic susceptibility, $S^M = -K \times 10^{-7}$, the value of K as determined experimentally by Pascal (222) is 864 and the specific susceptibility, $\chi_s = -0.496$. Slator (266) and Slator and on Twiss (267) de-

terminated the velocity of reaction of ethyl bromoacetate and sodium thiosulfate at 15°C. as 2.36, and at 25°C. as 6.4. Backer and von Mels (17) determined the value of K of ethyl bromoacetate with potassium sulfite at 25°C. in 40 per cent ethyl alcohol as 18.3. Clarke (63) determined the velocity of reaction of ethyl bromoacetate with pyridine at 55°C. as 1.004. Drushel and Hill (82) determined the rate of hydrolysis of ethyl bromoacetate in 0.5 N hydrobromic acid at 25°C. as 23.8. The activity of ethyl bromoacetate by the velocity coefficient of the reaction with silver nitrate at 49.9°C. is $K \times 10^4 = 0.208$ (258).

Clarke (64) derived the values in table 4 when amines were added to an absolute alcoholic solution of ethyl bromoacetate at 0°C.:

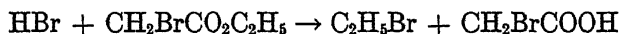


Aronstein (11) heated ethyl bromoacetate with ethyl bromide; the principal products were ethylene, hydrobromic acid, and bromoacetic acid.

TABLE 4
Reaction velocity constants

BASE	VALUES OF 10% WHEN n IS					
	2	3	4	5	6	7
$\text{C}_2\text{H}_5(\text{CH}_2)_n\text{N}(\text{CH}_3)_2$	11.4	10.7	10.3	11.2	10.9	
$(\text{CH}_2)_2\text{CH}(\text{CH}_2)_n\text{N}(\text{CH}_3)_2$	9.7	9.9	10.6	10.6		
$(\text{CH}_2)_2\text{N}(\text{CH}_2)_n(\text{CH}_3)_2$	9.5	16.8	24.9	20.8	24.5	27.5
$\text{CH}_3\text{O}(\text{CH}_2)_n\text{N}(\text{CH}_3)_2$	6.7	9.3	10.6	10.5	11.5	

The ethyl bromide was decomposed into ethylene and hydrobromic acid and this latter acted on the ethyl bromoacetate as follows:



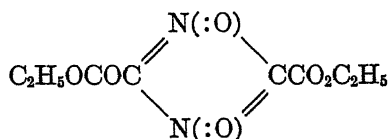
Upon distilling in a vacuum the product resulting from the action of sodium on hot ethyl bromoacetate there results the triethylester of aconitic acid (23).

By means of magnesium iodide in ethereal solution, ethyl bromoacetate is converted into ethyl iodoacetate, $\text{CH}_2\text{ICO}_2\text{C}_2\text{H}_5$ (40, 41).

Upon heating an alcoholic solution of ethyl bromoacetate with potassium fluoride in a glass vessel there is formed potassium bromide, silicon tetrafluoride, and glycolic ester (285).

From the interaction of ethyl bromoacetate and silver nitrate the following are obtained: ethyl glycolate, $\text{CH}_2(\text{OH})\text{CO}_2\text{C}_2\text{H}_5$; ethyl ethoxyacetate; ethyl glycolate nitrate, $\text{C}_2\text{H}_5\text{OCOCH}_2\text{ONO}_2$; ethyl glycolate

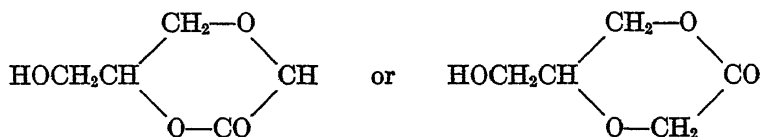
nitrite, $C_2H_5OCOCH_2ONO$; diethyloxalate; ethyloxynitriloformate, $C_2H_5OCOC\equiv N=O$, crystallizing from hot benzene in colorless needles, melting at $111-111.5^\circ C.$ and probably formed by the loss of one molecule of water from ethyldioxynitroacetate; ethyldioxycyano-gendicarboxylate a polymeride of the preceding compound, regarded as having the constitution



boiling at 158° (corrected) under 11 mm. and at $233-234^\circ C.$ at 760 mm. and reduced by tin and hydrochloric acid to aminoacetic acid; and a compound, $C_{12}H_{15}O_8N$, an oil boiling at $188-189^\circ C.$ at 11 mm., giving an amide by the action of strong ammonia, and regarded as having the constitution $C_3O_2N(CO_2C_2H_5)_3$ (249).

Ethyl bromoacetate reacts with dimethyl sulfide to form the ethyl ester of dimethylthetinbromide, $(CH_3)_2SBrCH_2CO_2C_2H_5$ (181).

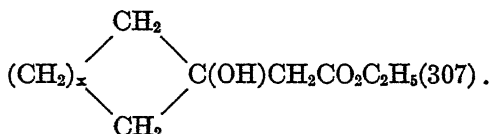
Glycerolxyacetolacetone,



is obtained from monosodium glycerol and ethyl bromoacetate; it is a viscid yellow oil, boiling at $170-175^\circ C.$ at 5 mm. (32).

Ethyl bromoacetate, when treated with zinc and methylheptenone, yields the ethyl ester of oxydihydrogeranic acid, $(CH_3)_2C:CH(CH_2)_2C(OH)-CH_3CH_2CO_2C_2H_5$ (292).

When a cyclic ketone is condensed with ethyl bromoacetate and zinc, an hydroxy ester of the following type results:



Ethyl β -hydroxy- β , β -diphenylpropionate, $HOC(C_6H_5)_2CH_2CO_2C_2H_5$, is readily obtained by the action of dilute acid on the product formed by the condensation of benzophenone, ethyl bromoacetate, and zinc in the presence of benzene. It crystallizes from dilute alcohol in glistening prisms,

m.p. 87°C . Ethyl β -methylcinnamate, $\text{C}_6\text{H}_5\text{C}(\text{CH}_3):\text{CHCO}_2\text{C}_2\text{H}_5$, is formed directly from acetophenone, ethyl bromoacetate, and zinc (242).

Ethyl diacetoacetate, $(\text{CH}_3\text{CO})_2\text{CHCO}_2\text{C}_2\text{H}_5$, is produced by the interaction of finely divided zinc, acetic anhydride, and ethyl bromoacetate in the presence of ether; ethyldipropionyl acetate, $(\text{C}_2\text{H}_5\text{CO})_2\text{CHCO}_2\text{C}_2\text{H}_5$, is produced in a similar manner by the use of propionic anhydride; ethyldibutyrylacetate, $(\text{C}_2\text{H}_5\text{CH}_2\text{CO})_2\text{CHCO}_2\text{C}_2\text{H}_5$, from butyric anhydride (190).

The reaction between ethyl bromoacetate and magnesium in ethereal solution leads to the formation of ethyl acetoacetate and of ethyl γ -bromoacetoacetate (283).

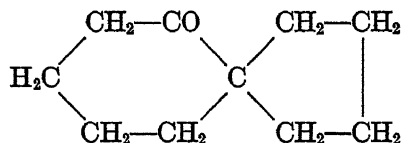
When attempts were made to prepare monobromoacethydroxamic or monoiodoacethydroxamic acids by the action of free hydroxylamine upon ethyl bromoacetate or ethyl iodoacetate unexpected complications arose, owing to the fact that hydroxylamine reacted with the halogen so readily that immediately after mixing the alcoholic solutions of ester and amine, crystalline precipitates formed which were found to be basic hydroxylammonium salts, $\text{NH}_2(\text{OH})_2\cdot\text{HBr}$ and $\text{NH}_2(\text{OH})_2\cdot\text{HI}$. Various other products, including small amounts of the desired hydroxamic acids, accompanied these salts, among them a crystalline compound, which contained no halogen. It melted at 65°C . and possessed the empirical formula, $\text{C}_8\text{H}_{15}\text{O}_5\text{N}$; it is probably a β,β -disubstituted hydroxylamine of the formula $\text{HON}:(\text{CH}_2\text{COC}_2\text{H}_5)_2$ (158).

The action of zinc and ethyl bromoacetate on ethyl orthoformate produces a product which, on saponification, results in β -ethoxyacrylic acid, $\text{C}_2\text{H}_5\text{OCH}:\text{CHCOOH}$ (299), which crystallizes in colorless prisms, m.p. 110.5°C ., and is identical with Otto's ethoxyacrylic acid (218).

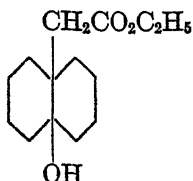
When hydrogen and ethyl bromoacetate are conducted over nickel heated to $250\text{--}300^{\circ}\text{C}$., there is formed principally ethyl acetate but also hydrogen bromide and a little acetaldehyde (245).

By the action of hydrazine hydrate on ethyl bromoacetate, nitrogen is evolved and the whole of the halogen is obtained in an ionic condition (74).

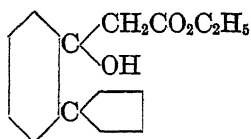
When ethyl bromoacetate is heated with cyclohexene oxide and zinc in benzene for six hours, ethyl 2-hydroxycyclohexylacetate is formed; it boils at 114°C . at 13 mm. The oxide of $\Delta^9,^{10}$ -octalin, ethyl bromoacetate, and zinc heated for six to seven hours in benzene gives 2-ketocyclohexane-spirocyclopentane,



boiling at 95°C. at 14 mm., and the ester,

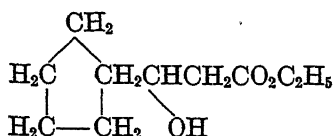


a viscous liquid with a peculiar sweetish smell, boiling at 125°C. at 0.1 mm. When 2-ketocyclohexanespirocyclopentane, ethyl bromoacetate, and zinc are heated in benzene for five hours the compound,

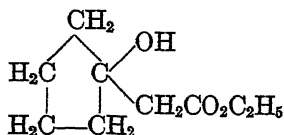


is formed; b.p. 135°C. at 0.25 mm. (65).

When cyclopentane aldehyde, ethyl bromoacetate, and zinc wool are heated in anhydrous benzene on a water bath for three hours the ester, ethyl β -hydroxy- β -cyclopentylpropionate, b.p. 117°C. at 14 mm., is formed



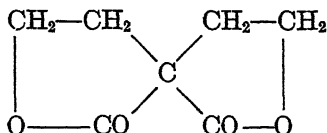
When cyclopentene oxide, ethyl bromoacetate, and zinc wool in dry benzene were heated on a water bath for three hours, a sweet-smelling ester, b.p. 108°C. at 18 mm. resulted, which gave a hydrazide, crystallizing in shining platelets from ethyl acetate, and melting at 143°C. Cyclopentanone, ethyl bromoacetate, and zinc wool in dry benzene when heated on a water bath gave ethyl cyclopentan-1-ol-1-acetate,



boiling at 108°C. at 18 mm.; with hydrazine hydrate, it gave a hydrazine, m.p. 143°C., identical with that obtained above (66).

When sodium ethylate in absolute alcohol at a temperature of 40°C. is treated with ethyl malonate and ethyl bromoacetate, sodium bromide pre-

cipitates and on concentrating the supernatant liquid there is obtained bis- γ -butyrolacetone- α,α -aspiran, in hexagonal plates, melting at 109–110°C. (183).



On heating ethyl bromoacetate to 150°C. for eight hours with mercury diethyl, there is formed ethylmercuric bromide, ethyl acetate, and ethylene (254, 255).

Ethyl bromoacetate has proved an excellent larvicide for screw-worms (33).

When zinc is allowed to react on a *p*-tolyl methyl ketone solution of ethyl bromoacetate the very unstable ethyl β -methyl-*p*-tolylethylenelactate, $\text{C}_6\text{H}_4(\text{CH}_3)\text{C}(\text{CH}_3)(\text{OH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ is obtained (195).

ETHYL IODOACETATE, $\text{CH}_3\text{ICO}_2\text{C}_2\text{H}_5$

Perkin and Duppa (230) first prepared ethyl iodoacetate by treating an alcoholic solution of ethyl bromoacetate with finely powdered potassium iodide and allowing the mixture to stand for several hours at 40–50°C. in the dark. Bodroux and Taboury (41) prepared ethyl iodoacetate in a similar manner; also by treating ethyl chloroacetate with an ethereal solution of magnesiumphenylamine iodide (36, 39, 40). Kekulé prepared the iodoacetate by the action of ethyl chloroacetate on an ethereal solution of potassium iodide (160); Tiemann (292) by the action of ethyl chloroacetate on an ethereal solution of magnesium iodide. By treating orthoiodoethylacetate with nitric acid and by heating an alcoholic solution of diiodoacetylene with excess alcoholic potassium hydroxide at 80–100°C., ethyl iodoacetate is formed (208). When glycol monoacetate or a mixture of glycol and acetic acid is saturated, in the cold, with hydriodic acid, ethyl iodoacetate is formed (265); also when ethyl bromoacetate is treated with sodium iodide for twenty-four hours at room temperature (100). Knoll and Company, on August 26, 1908, received German patent 230,172 for the production of ethyl iodoacetate from sodium iodide–acetone solution (167). Curtius and Hussong (74) prepared ethyl iodoacetate from ethyl diazoacetate by the action of dry hydrogen iodide in absolute ether and also by the action of hydrazine hydrate on ethyl bromoacetate. Perkin (227) prepared it by digesting ethyl chloroacetate with potassium iodide in alcohol. Ethyl chloroacetate reacts with the magnesium iodide derivative of *o*-toluidine in ethereal solution to form iodoaceto-*o*-toluidide but if, as

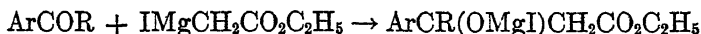
sometimes happens, the magnesium halogen compound undergoes spontaneous coagulation, the yield of iodoaceto-*o*-toluidide is very small, the chief product being ethyl iodoacetate (37, 38).

Ethyl iodoacetate is a colorless liquid with a pleasant odor but irritating and burning taste; it is practically unaffected by water (103). It boils at 69°C. at 12 mm., 73°C. at 16 mm. (208), 75–78°C. at 16 mm. (292), 85–86°C. at 25 mm. (40, 41), 95–96°C. at 43 mm. (130), 110°C. at 60 mm. (144), 142.5–143.5°C. at 250 mm. (corrected) (227), 178–180°C. (36, 54). Density: 4°/4°, 1.8320; 10°/10°, 1.8224; 15°/15°, 1.8150; 20°/20°, 1.8080; 25°/25°, 1.8013. Refractive index determinations: density, 12.7°/4°, 1.8173; η 12.7°/D = 1.50789; η 12.7°/ γ = 1.52683 (227); η 20°/D, 1.5072 (130). Magnetic rotation gave: t , 15.4°C.; specific rotation, 1.7784; molecular rotation, 11.652 (227). If the magnetic susceptibility $S^M = -K \times 10^{-7}$, the value of K was determined experimentally by Pascal (221, 222) as 1018 and calculated as 1011.5. Walden (306) found that no measurable electrolytic conductivity was to be observed in liquid sulfur dioxide. The velocity of reaction of ethyl iodoacetate with sodium thiosulfate at 15°C. is 2.55; at 25°C. it is 7.0 (266).

When equimolecular quantities of ethyl iodoacetate and methylethylaniline are mixed, a turbidity appears after about 2.5 hours. No heat of reaction is observed and there is a final contraction of about 6 per cent by volume, the viscosity of the suspended drops increasing as the volume of sirup increases. A periodic stratification of colored zones appears at intervals of twenty-four hours and persists for one or two months unless diffusion gradually renders the interface less sharp. The stratification is intensified when the tube is surrounded with silver. The phenomenon is regarded as due to the nature of the material, in particular to the nitrogen atoms, and not to external factors (105).

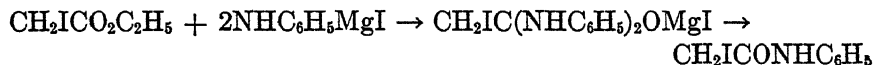
Ethyl iodoacetate easily decomposes in light with the liberation of iodine (230), also when warmed with alkalis (54) and when heated with nitric acid (208). With alcoholic sodium ethylate in the cold it gives ethoxyethyl acetate (208). When ethyl iodoacetate is heated to 230°C. with ethyl iodide, ethyl acetate and ethylene iodide (11, 12) are formed. Ethyl iodoacetate is converted by means of ethyl sulfide into ethyl methylthioglycolate, $\text{CH}_3\text{SCH}_2\text{CO}_2\text{C}_2\text{H}_5$, which with a slight excess of ethyl iodoacetate forms ethyl thiodiglycolate, $\text{S}(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)_2$ (182). When methylheptenone is condensed with ethyl iodoacetate in the presence of zinc, and the product is decomposed by water, a colorless oil of the composition, $\text{C}_{10}\text{H}_{17}\text{O}_3\text{C}_2\text{H}_5$, is obtained which is ethyl dihydrogeranate (22). Ethyl β -methylcinnamate, $\text{C}_6\text{H}_5\text{C}(\text{CH}_3):\text{CHCO}_2\text{C}_2\text{H}_5$, is prepared by condensing acetophenone with ethyl iodoacetate by means of magnesium or zinc (252, 295, 296). This is now a general method for the preparation of β -alkyl-

cinnamic acids (253); ketones interact with ethyl iodoacetate and magnesium in benzene solution according to the equation:



The β -arylalkyl hydracrylic acids, $\text{ArCR(OH)CH}_2\text{COOH}$ are obtained by decomposing the magnesium compound with water and then saponifying the ester; methyl *p*-tolyl ketone forms *p*, β -dimethylcinnamic acid, $\text{C}_6\text{H}_4(\text{CH}_3)\text{C}(\text{CH}_3):\text{CHCOOH}$; propiophenone forms β -phenyl- β -ethylhydracrylic acid, $\text{HOC}(\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5)\text{CH}_2\text{COOH}$; butyrophenone forms β -*n*-propylcinnamic acid, $\text{HOC}(\text{C}_3\text{H}_7):\text{CHCOOH}$; isovalerophenone forms β -phenyl- β -isobutylhydracrylic acid, $\text{CH}(\text{CH}_3)_2\text{CH}_2\text{C}(\text{C}_6\text{H}_5)-(\text{OH})\text{CH}_2\text{COOH}$; phenyl amyl ketone forms β -*n*-amylcinnamic acid, $\text{C}_5\text{H}_{11}\text{C}(\text{C}_6\text{H}_5):\text{CHCOOH} \cdot \text{H}_2\text{O}$.

When ethyl iodoacetate is allowed to act on magnesiumaniline iodide, in the presence of sufficient ether to keep the latter in solution, iodoacetanilide is formed (41, 42):



When ethyl iodoacetate is heated to 40°C. for several hours in the presence of iodine and zinc the compound, $\text{I}_3\text{Zn}_2(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)_3$, is formed (91); tin reacts similarly, so that when ethyl iodoacetate, iodine, and tin are heated to 60–70°C. for several hours the compound, $\text{SnI}_2(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)_2$ is formed (90).

By the action of hydrazine hydrate on ethyl iodoacetate, nitrogen is evolved and the whole of the halogen is obtained in an ionic condition (74).

Chlopin (58) determined ethyl iodoacetate as being 1.3 times more toxic than chlorine.

TRICHLOROMETHYL CHLOROFORMATE, PERCHLOROMETHYL FORMATE, ClCOOCCl_3

This is called diphosgene by the British and surpalite by the French.

In the dark chlorine acts only very slightly on methyl formate, even at the boiling point, but in the sunlight action is rapid at ordinary temperatures. If the current of chlorine is continued as long as the gas is absorbed, trichloromethyl chloroformate, ClCOOCCl_3 , is the main product (147).

Hood and Murdock (151) prepared diphosgene after the method of Hentschel (147) and found that the chlorination took place in steps, methyl formate being formed first and then successively the monochloro-, dichloro-, and trichloromethylchloro derivatives. Methyl formate reacts readily with chlorine in the dark, giving methyl chloroformate; further chlorination

in the dark, without the aid of an accelerating agent, gives some chloromethyl chloroformate, but the reaction velocity is low and the yield poor.

Kling, Florentin, Lassieur, and Schmutz (163) condensed carbonyl chloride with methyl alcohol to give methyl chloroformate which, when acted on by chlorine in sunlight, gives chloromethyl chloroformate, then dichloromethyl chloroformate, and finally the trichloromethyl ester.

Grignard, Rivat, and Urbain (126) found that light exerted a marked influence on the chlorination of methyl chloroformate: in diffused light it is only the chloromethyl ester which is formed, bright sunlight being necessary for the formation of the di- or tri-chloromethyl ester. In ultra-violet light the trichloro ester is easily obtained. The effect of temperature is such that up to 110–112°C. the chlorination proceeds smoothly, but at 113–114°C. it slackens very noticeably, and at 117°C. decomposition begins to take place with the formation of carbonyl chloride.

Trichloromethyl chloroformate is a colorless oily liquid with a fairly pleasant, sweet odor; it boils at 49°C. at 50 mm. (164), 125–126°C. at 748 mm. (127, 284), 127°C. at 750 mm. (7, 164), 127–128°C. (170), 127.5–128°C. (147). Its specific gravity is 1.64 at 14°C. (151), 1.6525 at 14°C. (147), 1.653 at 15°C. (90), 1.644 at 15°C. (127). Its vapor density is 6.636 (air = 1) (147). Its vapor pressure is 2.4 mm. at 0°C., 10.3 mm. at 20°C. (151, 284). One cubic meter of air at 20°C. becomes saturated with 26 g. of trichloromethyl chloroformate (7). Its volatility is 43,000 mg. per cubic meter (284).

The thermal decomposition of diphosgene was studied from 260°C. to 310°C. at pressures of 4 to 17 mm. It is of the first order and homogeneous except for a slight wall effect. The rate constant is given by k as $1.4 \times 10^{13} e^{-14,500/RT}$ (236).

When heated to 300–350°C. diphosgene decomposes, yielding carbon oxychloride in the ratio of 1 mole to 2; but this may be the result of catalytic action. Hentschel (147) states that when it is boiled with refluxing, it breaks down to some extent to phosgene, but Hood and Murdock (151) found practically no loss of weight when a sample of diphosgene was refluxed at the boiling point for fifteen hours. Since diphosgene reacts with alcohol, it is possible that Hentschel's results were due to uncondensed diphosgene vapor passing through the condenser (151).

It is not possible to synthesize diphosgene either from phosgene or from carbon dioxide and carbon tetrachloride by means of alumina or ferric oxide (151).

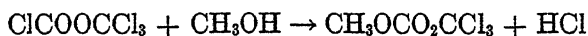
The solubility of nitrogen peroxide in diphosgene seemed to be of the same order as in tetrachlorodinitroethane, i.e., 30 cc. of dry nitrogen peroxide in 15.7 g. of $C_2Cl_4(NO_2)_2$ at 0°C. (9).

Diphosgene is hydrolyzed slowly by water at ordinary temperature and

fairly rapidly at 100°C., the products being hydrogen chloride and carbon dioxide:



Boiling with an aqueous solution of sodium hydroxide for 30 minutes decomposes it completely. It reacts with methyl alcohol in the cold to give trichloromethyl methoxyformate, $\text{CH}_3\text{OCO}_2\text{CCl}_3$,



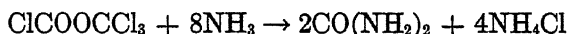
This reaction evolves heat and at a higher temperature the following reaction is obtained:



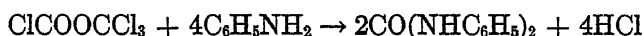
If there is an excess of alcohol, methyl chloroformate is formed,



Ammonia reacts rapidly with diphosgene vapor, forming urea and ammonium chloride,



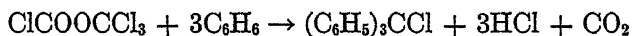
Aniline reacts to form carbanilide, which is insoluble in water,



and the carbanilide may react with more diphosgene according to the equation:



Diphosgene does not react directly with benzene but forms triphenylcarbinol chloride in the presence of aluminum chloride when heated to 150° C. in closed tubes:



When silver or sodium nitrite is treated with diphosgene, phosgene, nitrogen dioxide, nitrogen tetroxide, carbon dioxide, and the chlorides of the metal are obtained.

The catalytic decompositions of diphosgene are extremely interesting; alumina decomposes it to carbon dioxide and carbon tetrachloride, while ferric oxide splits it into phosgene. Purified charcoal behaves like iron oxide, but is more active. Vanadium oxide causes a slow decomposition, while uranium oxide causes a more rapid decomposition than does iron oxide (151). In the army canister, diphosgene is decomposed to phosgene

by the charcoal and it, in turn, is converted into hydrogen chloride and carbon dioxide; the soda lime decomposes diphosgene also to a very slight extent (151).

With dimethylaniline and benzaldehyde, diphosgene yields a green, with dimethylaniline a violet color-base (147).

With alcohol and phenol, trichloromethyl chloroformate yields trichloromethyl methyl carbonate, $\text{CH}_3\text{OCOOCCL}_3$, and phenyl chloroformate, $\text{ClCOOC}_6\text{H}_5$, respectively, while it is practically without action on unsaturated hydrocarbons, such as ethylene and amylene, when heated with them in sealed tubes (148).

Trichloromethyl chloroformate reacts with methyl alcohol to yield methyl trichloromethyl carbonate, and with ethyl and isoamyl alcohols to yield respectively the corresponding ethyl ester, b.p. 78°C . at 19 mm., density $20^\circ/4^\circ$, 1.4205; and the isoamyl ester, b.p. 120°C . at 23 mm., density $20^\circ/4^\circ$, 1.2644. Sodium phenoxide reacts with trichloromethyl chloroformate to yield phenyl trichloromethyl carbonate, m.p. 70.5°C . (211).

The initial product from equimolecular quantities of trichloromethyl chloroformate and an alcohol is the alkyl trichloromethyl carbonate (ROCOOCCL_3). The following have been isolated: *n*-propyl, b.p. 93°C . at 12 mm., density $20^\circ/4^\circ$, 1.359, η^{20} , 1.4451; isobutyl, b.p. 103°C . at 14 mm., density $20^\circ/4^\circ$, 1.302, η^{20} , 1.4446; β -chloroethyl, b.p. 110°C . at 12 mm., 115°C . at 16 mm., density $20^\circ/4^\circ$, 1.5664, η^{20} , 1.4748; allyl, b.p. $89-90^\circ\text{C}$. at 11 mm., density $20^\circ/4^\circ$, 1.4015, η^{20} , 1.4590 (212).

Trichloromethyl chloroformate and the compounds containing the OCCl_3 group react with amines as do alcohols and phenols, giving the same end products as in the reaction with phosgene:



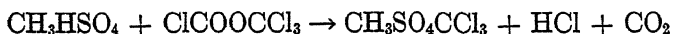
The mechanism of the reaction without formation of intermediate products is not clear and is being investigated. An ester solution of diphosgene with cooling and shaking was added to an ethereal solution of *p*-nitroaniline with the formation of *sym*-dinitrophenylcarbamide, $\text{CO}(\text{NHC}_6\text{H}_4\text{NO}_2)_2$, and the unstable trichloromethyl-*p*-nitrophenylurethan



yellow crystals evolving phosgene. An ether solution of perchloromethylformate was added to an ethereal solution of diphenylamine with the formation of trichloromethyldiphenylphenylurethan, $\text{CO}(\text{OCCl}_3)\text{N}(\text{C}_6\text{H}_5)_2$, m.p. 61°C . (198).

The action of trichloromethyl chloroformate on carbonic and alkyl-

sulfuric acids gives the corresponding chloroanhydrides, the reaction proceeding possibly thus:



and



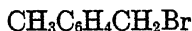
When a cold mixture of diphosgene and methyl sulfate was heated to 65°C., the turbulent reaction regulated at 20–25°C., the mixture then heated again 4 hours on a boiling water bath, then distilled *in vacuo* with anhydrous Na_2SO_4 , methyl chlorosulfonate, ClSO_3CH_3 was produced. A mixture of benzoic acid and diphosgene heated eight hours at 95–105°C. produces benzoyl chloride (170).

Hood and Murdock (151) found the lethal concentration of diphosgene for dogs as 0.25 mg. per liter (40 parts per million) for 30 minute exposure.

The toxic effect of the different chloromethyl carbonates and chloroformates on rabbits, guinea pigs, and dogs was examined, the animals inhaling the vapors diluted with air. The chloromethyl chloroformates become more and more toxic as the number of chlorine atoms introduced increases. For the same number of chlorine atoms present in the molecule the chloroformates are more toxic than the carbonates (197). The relative toxicity, compared to chlorine, taken as unity, is 27 (58).

When diphosgene is introduced into the lungs of dogs, polypnea results (98).

XYLYL BROMIDE, BROMODIMETHYLBENZENE, TOLYL BROMIDE,



Xylyl bromide is prepared by the action of bromine on boiling xylene (*o*-, *m*-, or *p*-) (14, 235), or by the action of bromine on the three xylenes in sunlight (251). Haller and Bauer (132) prepared the *o*- and *m*-xylyl bromides by treating the vapor of *o*- and *m*-xylenes with bromine. Pavlovskii (224) prepared the *o*- and *p*-xylyl bromides and Zeltner and Tarassow (315) the latter by boiling the corresponding ditolubenzyl ethers, $(\text{CH}_3\text{C}_6\text{H}_4\text{CH}_2)_2\text{O}$, with excess hydrobromic acid (density, 1.49) in tubes. Emde (87) prepared *o*-xylyl bromide by treating *o*-xylene with bromine. Colson (71) prepared *o*- and *m*-xylyl bromides by treating the corresponding xylene glycol, $\text{CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{OH}$, with bromine. Titley (298) prepared *m*- and *p*-xylyl bromides by treating the corresponding hydrocarbons with dry bromine for six hours at 130°C. *m*-Xylyl bromide was prepared by treating a carbon tetrachloride solution of *m*-xylene with a bromine-carbon tetrachloride solution and keeping the mixture cold (196). Hoch (149) prepared *o*-xylyl bromide by treating the corresponding ethyl ether with hydrobromic acid (density, 1.48).

All forms are soluble in alcohol, ether, and chloroform but insoluble in water.

Properties of o-xylyl bromide

Prisms; m.p. 20°C. (262), 21°C. (235); b.p. 102°C. at 11 mm. (262), 108°C. at 16 mm. (132), 215–218°C. (14), 215–220°C. (224), 216–217°C. at 742 mm. (235), 220°C. (71), 223–224°C. (corrected) at 761 mm. (87). Density: 1.3811 at 23°C. (235). The rate of reaction with dimethylaniline at 40°C. is 1.315×10^4 , and with triisoamylamine at 40°C. is 3.4×10^0 (233).

On boiling with alcohol there is formed ethyl-*o*-xylyl ether, $\text{CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{OC}_2\text{H}_5$, a liquid with a peppermint-like odor, b.p. 208–210°C. (47). On addition of magnesium in ether there is formed principally the product *sym*-di-*o*-tolylethane (55, 56). On treatment of alcoholic potassium cyanide, *o*-xylyl bromide is converted into the corresponding nitrile (14).

Properties of m-xylyl bromide

Colorless liquid with a penetrating odor (132); b.p. 97–99°C. at 8 mm. (262), 100–101°C. at 14 mm. (298), 105°C. at 13 mm. (132), 110–115°C. at 20 mm. (298), 185°C. at 340 mm. (232), 200–205°C. (196), 212°C. (71), 212–215°C. (14, 235). Density: 1.3711 at 23° (235). The rate of reaction with dimethylaniline at 40° is 8.625×10^4 ; with triisoamylamine at 40°C. is 2.7×10^0 (233).

On addition of magnesium in ether the principal product is α,β -di-*m*-tolyl ethane (55, 56). When treated with potassium cyanide in dilute alcohol, *m*-tolylacetonitrile is formed (14, 196, 298).

Properties of p-xylyl bromide

Needles; m.p. 31°C. (61), 35°C. (132, 224, 315), 35.5°C. (14, 235, 251, 262, 298); b.p. 100°C. at 9 mm. (262), 100°C. at 10 mm. (132), 216–224°C. (224), 218–220°C. at 740 mm. (235, 251). Density: 1.3237 at 20°C. (235). The rate of reaction with dimethylaniline at 40°C. is 2.325×10^4 ; with triisoamylamine at 40°C. is 6.6×10^0 (233); with aniline at 30.5°C. is 87; with pyridine at 30.5°C. is 9.5 (19).

On addition of magnesium in ether to xylyl bromide there is formed principally 4,4'-dimethyldibenzene (55, 56). When xylyl bromide is boiled with potassium cyanide dissolved in dilute alcohol, *p*-tolylacetonitrile is formed (14). By heating for 1.5 hours under reflux with acetic acid and potassium acetate the resulting *p*-tolylcarbiny acetate is formed, and when boiled with 10 per cent sodium hydroxide it is converted into *p*-tolylcarbinol (157). By heating an acetic anhydride solution of *p*-xylyl bromide

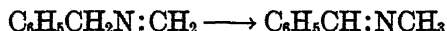
with fuming nitric acid in acetic anhydride there is formed ω -bromo-3-nitro-*p*-xylene (157).

It was anticipated by Shoesmith and Slater (262) as the result of the study by Lapworth and Shoesmith (177), Shoesmith (259), and Shoesmith, Hetherington, and Slater (260) on the influence which oxygen exerts on halogen atoms in various benzoid compounds that the monobromoxylenes in the case of hydrolysis should be $p > o > m$ and of reduction by hydriodic acid should be $m > o > p$. Table 5 substantiates the former prediction. The three xylyl bromides combine directly with hexamethylenetetramine in chloroform solution to give the additive compounds, $C_6H_{12}N_4BrCH_2C_6H_4CH_3$, having melting points, respectively, as follows: *o*-, 198°C.; *m*-, 215°C.; *p*-, 216°C. Each of these is similarly decomposed by boiling with water, giving the corresponding tolualdehydes. The course of this decomposition reaction is not clear, but the relatively abundant production of methylamine points to the possible primary production

TABLE 5
Hydrolysis of bromoxylenes at 60°C. (262)

<i>t</i> <i>minutes</i>	PERCENTAGE CHANGE		
	ortho	meta	para
30	55	25	66
60	77	42	87
120	89	64	96
180	94	77	100

of benzylmethyleamine, which undergoes isomerization to benzylidene-methylamine (272).



Treatment of the sodium derivative of phenyl isopropyl ketone with xylyl bromides gives the corresponding xylyldimethylacetophenones, $C_6H_5COC(CH_3)_2CH_2C_6H_4CH_3$. Boiling points: *o*-, 199–200°C. at 15 mm.; *m*-, 196–197°C. at 12 mm.; *p*-, 200–202°C. at 13 mm. (132).

Upon saponifying *o*- or *m*-xylyl bromide with a large excess of potassium carbonate solution, tolylcarbinol, $C_6H_4(CH_3)CH_2OH$, is obtained: *o*-, white crystals, m.p. 34.2°C., soluble in 100 parts water at 12°C., b.p. 216–217.5°C.; *m*-, liquid, b.p. 216–217.5°C. at 758 mm., density 1.028 at 12°C., soluble in 80 to 100 parts water at 12°C. (71).

Xylyl bromides are destroyed very slowly by water (103).

p-Xylyl bromide reacts with benzyl-*p*-methylbenzylmethylamine to form

the additive compound, *p*-methylbenzyltrimethylammonium bromide, m.p. 184°C. (48).

All species of flies under observation were strongly repelled by xylyl bromides (33).

PHYSIOLOGICAL ACTION AND PATHOLOGY

Men exposed to the action of chloroacetophenone (the physiological action of other non-toxic lachrymators is practically the same) exhibit the following symptoms: irritation of the eyes, lachrymation, and burning of the more tender portions of the skin. In some cases there is a tendency toward increased salivation and irritation of the throat. Following exposure there may be some discomfort, but this is of relatively short duration, except in the case of exposure to very high concentration or to low concentrations for prolonged periods. In these latter cases it may require twenty-four hours for the eyes to feel normal again. Men exposed experimentally to high concentrations for short periods of time were unable to open their eyes for several minutes after exposure. In some cases a conjunctivitis was observed which lasted several hours.

Chloroacetophenone has comparatively little effect on the skin of either man or animals. When applied in excess to the human skin, there is a burning sensation, slight rubefaction, and sometimes small vesicles appear. This inflammation subsides in about seven days. In vapor form the inflammation produced is very mild and is usually quite unimportant, although in exceptionally sensitive individuals it may prove quite harassing. Chloroacetophenone has no effect on the lungs of man in any concentration that will be met with in the field.

Dogs exposed to the toxic action of chloroacetophenone exhibit great excitement, irritation of the eyes, nose, and throat, lachrymation, salivation, nasal discharge, and dyspnea. Vomiting, trembling, and twitching of the limbs may occur. Following exposure, there is usually a decided corneal involvement—varying from a slight opacity to ulceration and blindness—soreness of the throat, and coughing. A few dogs that died showed congestion and edema of the lungs, a true membranous tracheitis, and decided corneal opacity. It is quite impossible that the concentrations used on these animals should ever be encountered in the field. It is stated that horses are quite resistant to chloroacetophenone and show no evidence of irritation or lachrymation.

Two fatal cases of poisoning by a lachrymator have been recorded. Shufflebotham (263) reports the case of a workman who was gassed by the explosion of a shell containing ethyl iodoacetate and died on the same day from severe inflammation of the trachea and lungs. In this case edema was not marked, but in parts of the lungs the alveoli were packed with

extravasated red corpuscles. A second fatal case of ethyl iodoacetate poisoning occurred in France to a member of a trench mortar crew owing to the premature explosion of a bomb (216). The post-mortem examination showed pulmonary edema with multiple small hemorrhages in the lungs.

TREATMENT

Treatment consists in merely washing the eyes with a solution of boric acid or sodium bicarbonate. As these lachrymators cause no permanent damage to the eyes, and only transient discomfort, even this treatment is generally unnecessary. The mask affords perfect protection against these lachrymators, and with the mask properly adjusted a man can go through the densest fumes in perfect comfort. However, the effect of lachrymators is practically instantaneous, and some discomfort may be experienced before the mask can be adjusted. The natural instinct when a lachrymator is felt is to turn and run. This is what makes these agents so very effective against mobs and for other police purposes. The first instinct of a soldier with a mask should be to put it on; this is only acquired by training, and when that training has been effective the mask should be on and properly adjusted in 7 seconds after the first warning of gas.

PATENTS

Numerous patents have been issued for the means of dispersing lachrymatory gases: Oglesby and Ehrenfeld on February 14, 1926 received U. S. patent 1,659,158 for a device for dispersing lachrymatory irritants by heat from associated combustible material (217); Ranken and Nobel Industries, Ltd., on February 13, 1926 received British patent 275,830 for a lachrymatory torch (237); Ranken and Nobel Industries, Ltd., on February 13, 1926 received British patent 276,279 for a device for producing lachrymatory and like gases for military purposes (237); Flury received U. S. patent 1,712,917 for a fumigant comprising hydrocyanic acid and some lachrymatory warning substance (102); Alden (1) received U. S. patent 1,735,522 for a tear gas projectile; Goss (123) U. S. patent 1,750,101 for a formula for lachrymatory gas; Minto (202) U. S. patent 1,877,773 for a tear gas cartridge.

REFERENCES

- (1) ALDEN: Chem. Abstracts **24**, 728 (1930).
- (2) ALEKSEEVSKII AND ALEKSEEV: Zhur. Prikladnoi Khim. **1**, 194-200 (1928).
- (3) ALLEN AND TRIGG: Ind. Eng. Chem., News Ed. **9**, 184 (1931).
- (4) AMINOFF: Arkiv Kemi Mineral Geol. [4] **6**, 1-15 (1916).
- (5) ANDREICH AND LeBLANC: Z. wiss. Phot. **15**, 148-64, 183-96, 197-223 (1915).
- (6) ANON: Public Health Repts. **37**, 2744-7 (1922).
- (7) ANON: Gasschutz and Luftschutz **2**, 264 (1932).

- (8) ARBUSOW: Ber. 40, 3301-4 (1907).
- (9) ARGO, JAMES, AND DONNELLY: J. Phys. Chem. 23, 578-85 (1919).
- (10) ARNDT, AMENDE, AND ENDER: Monatsh. 59, 202-19 (1932).
- (11) ARONSTEIN: Ber. 14, 606-7 (1881).
- (12) ARONSTEIN AND KRAMPS: Ber. 13, 489-91 (1880).
- (13) ASTRUC AND MURCO: Compt. rend. 131, 943-5 (1900).
- (14) ATKINSON AND THORPE: J. Chem. Soc. 91, 1687-710 (1907).
- (15) AUWERS AND BERNHARDI: Ber. 24, 2209-33 (1891).
- (16) AUWERS AND JORDAN: Ber. 58, 26-35 (1925).
- (17) BACKER AND VON MELS: Rec. trav. chim. 49, 363-80 (1930).
- (18) BAKER: J. Chem. Soc. 1932, 1148-57.
- (19) BAKER: J. Chem. Soc. 1932, 2631-6.
- (20) BANCROFT: J. Phys. Chem. 12, 417-47 (1908).
- (21) BARBAGLIA: Ber. 7, 467-9 (1874).
- (22) BARBIER AND BOUVEAULT: Compt. rend. 122, 393-5 (1896).
- (23) BAYER: Ann. 135, 306-12 (1865).
- (24) BÉHAL AND DETOEUF: Compt. rend. 153, 1229-31 (1911).
- (25) BEILSTEIN: Ann. 143, 369-72 (1867).
- (26) BELLAY AND HOUDARD: Compt. rend. 170, 236-8 (1920).
- (27) BENDER: Ber. 21, 2492-8 (1888).
- (28) BERTRAND: Compt. rend. 171, 965-7 (1920).
- (29) BERTRAND AND ROSENBLATT: Compt. rend. 168, 911-3 (1919).
- (30) BISCHOFF: Ber. 5, 863-7 (1872).
- (31) BISCHOFF: Ber. 8, 1329-44 (1875).
- (32) BISCHOFF: Ber. 40, 2803-13 (1907).
- (33) BISHOPP, ROARK, PARMAN, AND LAAKE: J. Econ. Entomol. 18, 776-8 (1925).
- (34) BODFORSS: Ber. 52, 142-5 (1919).
- (35) BODFORSS: Ber. 52, 1762-75 (1919).
- (36) BODROUX: Compt. rend. 140, 1597-8 (1905).
- (37) BODROUX: Compt. rend. 141, 195-6 (1905).
- (38) BODROUX: Bull. soc. chim. [3] 35, 519-20 (1906).
- (39) BODROUX AND TABOURY: Bull. soc. chim. [3] 33, 831-4 (1905).
- (40) BODROUX AND TABOURY: Compt. rend. 144, 1216-7 (1907).
- (41) BODROUX AND TABOURY: Bull. soc. chim. [4] 1, 909-14 (1907).
- (42) BODROUX AND TABOURY: Compt. rend. 144, 1437-8 (1907).
- (43) BRADNER: Chem. Abstracts 20, 465 (1926).
- (44) BRADNER: Chem. Abstracts 22, 999 (1928).
- (45) BRAUN, VON: Ber. 36, 2651-3 (1903).
- (46) BRAUN, VON: Ber. 40, 3933-43 (1907).
- (47) BRAUN, VON: Ber. 43, 1350-2 (1910).
- (48) BRAUN AND ENGEL: Ann. 436, 299-320 (1924).
- (49) BRAUN AND MÜLLER: Ber. 39, 2018-22 (1906).
- (50) BRENDLER AND TAFEL: Ber. 31, 2683-6 (1898).
- (51) BREUER AND ZINCKE: Ber. 13, 635-61 (1880).
- (52) BRUNER AND DLUSKA: Bull. acad. sci. Cracovie, pp. 691-730 (1907).
- (53) BÜLOW AND SEIDEL: Ann. 439, 48-58 (1924).
- (54) BUTLEROW: Ber. 5, 479 (1872).
- (55) CARRÉ: Compt. rend. 148, 1108-10 (1909).
- (56) CARRÉ: Bull. soc. chim. [4] 5, 486-9 (1909).
- (57) CHALANAY AND KNOEVENAGEL: Ber. 25, 295 (1892).

- (58) CHLOPIN: *Z. ges. Schiess-Sprengstoffw.* **22**, 227-30 (1927).
- (59) CHRZASCZEWSKA AND CHWALINSKI: *Roczniki Chem.* **7**, 67-73 (1927).
- (60) CHRZASCZEWSKA AND SOBIERANSKI: *Roczniki Chem.* **7**, 79-86 (1927).
- (61) CIESIELSKI: *Bull. acad. sci. Cracovie*, pp. 270-4 (1906).
- (62) CLAISEN: *Ber.* **38**, 693-709 (1905).
- (63) CLARKE: *J. Chem. Soc.* **97**, 416-29 (1910).
- (64) CLARKE: *J. Chem. Soc.* **103**, 1689-1704 (1913).
- (65) CLEMO AND ORMSTON: *J. Chem. Soc.* **1932**, 1778-83.
- (66) CLEMO AND ORMSTON: *J. Chem. Soc.* **1933**, 362.
- (67) CLIBBENS AND NIERENSTEIN: *J. Chem. Soc.* **107**, 1491-4 (1915).
- (68) CLOËZ: *Ann. chim.* [6] **9**, 145-221 (1886).
- (69) COHEN, DAWSON, AND CROSLAND: *J. Chem. Soc.* **87**, 1034-7 (1905).
- (70) COLLET: *Bull. soc. chim.* [3] **17**, 506-10 (1897).
- (71) COLSON: *Bull. soc. chim.* **43**, 6-8 (1885).
- (72) CONANT AND KIRNER: *J. Am. Chem. Soc.* **46**, 232-52 (1924).
- (73) CURTIUS: *J. prakt. Chem.* **38**, 430 (1888).
- (74) CURTIUS AND HUSSONG: *J. prakt. Chem.* **83**, 249-78 (1911).
- (75) DARZEN: *Compt. rend.* **139**, 1214-7 (1904).
- (76) DEAN AND BERCHET: *J. Am. Chem. Soc.* **52**, 2823-6 (1930).
- (77) DEMOLE: *Ann.* **173**, 117-23 (1874).
- (78) DENIGÈS: *Ann. chim.* [7] **18**, 382-432 (1899).
- (79) DESGREZ, GUILLERMARD, AND SAVES: *Compt. rend.* **171**, 1177-9 (1920).
- (80) DOBROSERDOFF: *J. Russ. Phys. Chem. Soc.* **43**, 73-130 (1911).
- (81) DOW: *Chem. Abstracts* **16**, 1998 (1922).
- (82) DRUSHEL AND HILL: *Am. J. Sci.* **30**, 72-8 (1910).
- (83) DUFRAISSE AND BONGRAND: *Compt. rend.* **171**, 817-9 (1920).
- (84) DUFOIT AND MAJOIU: *J. chim. phys.* **7**, 169-88 (1909).
- (85) DYCKERHOFF: *Ber.* **10**, 119-21 (1877).
- (86) DYCKERHOFF: *Ber.* **10**, 531-3 (1877).
- (87) EMDE: *Ann.* **391**, 88-109 (1912).
- (88) EMMERLING: *Ber.* **6**, 22-4 (1873).
- (89) EMMERLING AND WAGNER: *Ann.* **204**, 27-49 (1880).
- (90) EMMERT AND ELLER: *Ber.* **44**, 2328-30 (1911).
- (91) EMMERT AND ELLER: *Ber.* **46**, 1508-11 (1913).
- (92) ERREIRA: *Gazz. chim. ital.* **17**, 193-209 (1871).
- (93) EVLAMPYEV: *Ber.* **62**, 2386-91 (1929).
- (94) ÉWE: *Ind. Eng. Chem., News Ed.* **9**, 229 (1931).
- (95) FAVORSKII: *J. Russ. Phys. Chem. Soc.* **44**, 1339-95 (1912).
- (96) FAVORSKII AND ISATTSCHEKA: *J. Russ. Phys. Chem. Soc.* **44**, 1339-95 (1912).
- (97) FAVREL: *Bull. soc. chim.* **41**, 1494-7 (1927).
- (98) FEGLER: *Compt. rend. soc. biol.* **100**, 222-4 (1929).
- (99) FEIST: *Ber.* **35**, 1545-56 (1902).
- (100) FINKELSTEIN: *Ber.* **43**, 1528-32 (1910).
- (101) FLÜRSCHHEIM AND HOLMES: *J. Chem. Soc.* **1928**, 1607-16.
- (102) FLURY: *Chem. Abstracts* **23**, 3298 (1929).
- (103) FLURY AND RONA: *Z. ges. exptl. Med.* **13**, 16-30 (1921).
- (104) FOURNEAU AND TIFFENEAU: *Compt. rend.* **145**, 437-9 (1907).
- (105) FREUNDLER AND PILAUD: *Bull. soc. chim.* [4] **47**, 1151-7 (1930).
- (106) FRIEDEL AND CRAFTS: *Ann. chim.* [6] **1**, 449-532 (1884).
- (107) FRIEDLÄNDER: *Ber.* **10**, 1832 (1877).

- (108) FRIES AND WEST: Chemical Warfare. McGraw-Hill Book Co., New York (1921).
- (109) FRITSCH: Ber. **26**, 597-8 (1892).
- (110) FRITSCH: Ann. **279**, 310-9 (1894).
- (111) FURNÉE: Arch. Pharm. **236**, 343-53 (1898).
- (112) GABRIEL: Ber. **41**, 1127-56 (1908).
- (113) GABRIEL: Ber. **46**, 3859-61 (1913).
- (114) GABRIEL AND PINKUS: Ber. **26**, 2197-209 (1893).
- (115) GAL: Ann. **132**, 177-80 (1864).
- (116) GAL: Compt. rend. **71**, 272-4 (1870).
- (117) GAUTIER: Ann. chim. [6] **14**, 337-404 (1888).
- (118) GIUA AND RACCIU: Atti accad. sci. Torino Classe sci. fis. mat. nat. **67**, 409-12 (1932).
- (119) GLADSTONE AND TRIBE: J. Chem. Soc. **47**, 448-56 (1885).
- (120) GLUTZ: J. prakt. Chem. [2] **39**, 237 (1870).
- (121) GLUTZ AND FISCHER: J. prakt. Chem. [2] **4**, 52 (1871).
- (122) GOSS: Chem. Abstracts **20**, 3574 (1926).
- (123) GOSS: Chem. Abstracts **24**, 2216 (1930).
- (124) GRAEBE: Ber. **4**, 34-5 (1871).
- (125) GRAEBE: Ber. **9**, 798 (1876).
- (126) GRIGNARD, RIVAT, AND URBAIN: Compt. rend. **169**, 1074-7 (1919).
- (127) GRIGNARD, RIVAT, AND URBAIN: Compt. rend. **169**, 1143-7 (1919).
- (128) GUÉRIN: Ann. sci. agron. **38**, 10-9 (1921).
- (129) GUÉRIN AND LORMAND: Compt. rend. **170**, 401-3 (1920).
- (130) GUSTUS AND STEPHENS: J. Am. Chem. Soc. **55**, 378-86 (1933).
- (131) HALBAN AND GAST: Z. physik. Chem. **91**, 593-604 (1916).
- (132) HALLER AND BAUER: Compt. rend. **153**, 21-7 (1911).
- (133) HANSLIAN: Der chemische Krieg. (1930).
- (134) HANTZSCH: Ber. **23**, 1472-4 (1890).
- (135) HANTZSCH: Ber. **23**, 1474-6 (1890).
- (136) HANTZSCH AND WILD: Ann. **289**, 285-309 (1896).
- (137) HANZLIK AND TARR: J. Pharmacol. **14**, 221-8 (1919).
- (138) HEDELIUS: Z. physik. Chem. **96**, 343-66 (1920).
- (139) HELLON AND TCHERNIAC: Ber. **16**, 348-50 (1883).
- (140) HENRY: Ann. **156**, 174-81 (1870).
- (141) HENRY: Ber. **5**, 186-92 (1872).
- (142) HENRY: Ber. **5**, 965-8 (1872).
- (143) HENRY: Bull. acad. roy. méd. Belg. [3] **35**, 57-63 (1900).
- (144) HENRY: Rec. trav. chim. **20**, 243-54 (1901).
- (145) HENRY: Bull. acad. roy. méd. Belg. [3] **37**, 236-48 (1901).
- (146) HENRY: Compt. rend. **145**, 21-5 (1907).
- (147) HENTSCHEL: J. prakt. Chem. [2] **36**, 99-113 (1887).
- (148) HENTSCHEL: J. prakt. Chem. [2] **36**, 305-17 (1887).
- (149) HOCH: Compt. rend. **192**, 464-6 (1931).
- (150) HOLLEMAN AND POLAK: Rec. trav. chim. **27**, 435-54 (1908).
- (151) HOOD AND MURDOCK: J. Phys. Chem. **23**, 498-512 (1919).
- (152) HOOGEVEEN: Rec. trav. chim. **50**, 669-78 (1931).
- (153) HOOGEVEEN AND JANSEN: Rec. trav. chim. **51**, 260-4 (1932).
- (154) HUGHES, WATSON, AND YATES: J. Chem. Soc. **1931**, 3318-24.
- (155) HUNTER AND EDGAR: J. Am. Chem. Soc. **54**, 2025-8 (1932).

- (156) IMBERT: Chem. Abstracts 4, 235 (1910).
(157) INGOLD AND ROTHSTEIN: J. Chem. Soc. **1928**, 1278-89.
(158) JONES AND WERNER: J. Am. Chem. Soc. **39**, 413-22 (1917).
(159) KATZ AND TALBERT: Bur. Mines Tech. Paper No. 480 (1930).
(160) KEKULÉ: Ann. **131**, 221-38 (1864).
(161) KEKULÉ: Ann. **137**, 190-2 (1866).
(162) KLING: Ann. chim. [8] **5**, 471-559 (1905).
(162a) KLING: Bull. soc. chim. [3] **33**, 322-4 (1905).
(163) KLING, FLORENTIN, LASSIEUR, AND SCHMUTZ: Compt. rend. **169**, 1046-7 (1919).
(164) KLING, FLORENTIN, LASSIEUR, AND SCHMUTZ: Compt. rend. **169**, 1166-8 (1919).
(165) KNÖFFER: Monatsh. **31**, 87-110 (1910).
(166) KNOLL: Z. ges. Schiess-Sprengstoffw. **22**, 294-6 (1927).
(167) KNOLL AND Co.: Chem. Zentr. **1911**, I, 359.
(168) KORSCHUN: Ber. **37**, 2196-7 (1904).
(169) KORTEN AND SCHOLL: Ber. **34**, 1901-10 (1901).
(170) KRAFT AND ALEKSEEV: J. Gen. Chem. U. S. S. R. **2**, 726-9 (1932).
(171) KRASSUSKY: J. Russ. Phys. Chem. Soc. **33**, 1-6 (1901).
(172) KRIWASIN: Ber. **4**, 563 (1871).
(173) KRIWASIN: Z. Chem [2] **7**, 263-9 (1871).
(174) LAPWORTH: J. Chem. Soc. **83**, 1114-29 (1903).
(175) LAPWORTH: J. Chem. Soc. **85**, 30-42 (1904).
(176) LAPWORTH AND HANN: J. Chem. Soc. **81**, 1499-1508 (1902).
(177) LAPWORTH AND SHOESMITH: J. Chem. Soc. **121**, 1391-1400 (1922).
(178) LeBLANC AND ANDRICH: Z. Elektrochem. **20**, 543-7 (1914).
(179) LECAT: Ann. soc. sci. Bruxelles **45**, 169-76, 284-94 (1927).
(180) LEFEBURE: The Riddle of the Rhine. The Chemical Foundation, New York (1923).
(181) LETTS: Jahresbericht über die Fortschritte der Chemie, p. 685 (1878).
(182) LETTS AND COLLIE: Jahresbericht über die Fortschritte der Chemie, p. 685 (1878).
(183) LEUCHS AND GIESELER: Ber. **45**, 2114-29 (1912).
(184) LEVENE: Organic Syntheses **10**, 12-3. John Wiley and Sons, New York (1930).
(185) LINNEMANN: Ann. **125**, 307-18 (1863).
(186) LINNEMANN: Ann. **134**, 170-5 (1865).
(187) LINNEMANN: Ann. **138**, 122-6 (1866).
(188) LINNEMANN: Chem. Zentr. **21**, 388-90 (1874).
(189) LIPPMANN: Ber. **24**, 2489-91 (1912).
(190) LUNIAK: Ber. **42**, 4808-15 (1909).
(191) MANNICH AND HAHN: Ber. **44**, 1542-52 (1911).
(192) MARKOWNIKOFF: Ann. **208**, 355 (1881).
(193) MARKOWNIKOFF: Z. Chem. **1870**, 424.
(194) MATHESON AND HUMPHRIES: J. Chem. Soc. **1931**, 2514-6.
(195) MATZUREVICH: J. Russ. Phys. Chem. Soc. **41**, 56-66 (1909).
(196) MAXWELL AND ADAMS: J. Am. Chem. Soc. **52**, 2959-72 (1930).
(197) MAYER, MAGNE, AND PLANTFOL: Compt. rend. **172**, 136-9 (1921).
(198) MELNIKOV AND VINOKUROV: J. Gen. Chem. U. S. S. R. **2**, 484-90 (1932).
(199) MEYER: Ann. **380**, 212-42 (1911).
(200) MEYER: Der Gaskampf und die chemischen Kampfstoffe. S. Hirzel, Leipzig (1925).
(201) MIELENZ: Gasschutz und Luftschutz **2**, 10-4 (1932).

- (202) MINTO: Chem. Abstracts **27**, 355 (1933).
- (203) MORGULEVA: J. Russ. Phys. Chem. Soc. **46**, 235-46 (1913).
- (204) MORLEY AND GREEN: J. Chem. Soc. **47**, 132-4 (1885).
- (205) MUKHIN, GINZBURG, AND MOISEEVA: Ukrain. Khim. Zhur. **2**, 135-52 (1926).
- (206) MULDER: Ber. **5**, 1007-11 (1872).
- (207) NAUMANN: Ann. **129**, 257-81 (1864).
- (208) NEF: Ann. **298**, 202-374 (1897).
- (209) NEF: Ann. **335**, 247-333 (1904).
- (210) NEKRASOV: J. prakt. Chem. **119**, 108 (1928).
- (211) NEKRASOV AND MELNIKOV: J. Russ. Phys. Chem. Soc. **62**, 631-43 (1930).
- (212) NEKRASOV AND MELNIKOV: J. prakt. Chem. **127**, 210-8 (1930).
- (213) NIEMIŁOWICZ: Monatsh. **7**, 241-55 (1886).
- (214) NORTON AND WESTENHOFF: Am. Chem. J. **10**, 213-6 (1888).
- (215) OBRÉZIA: Ann. **266**, 324-58 (1891).
- (216) Official History of the War, Vol. II, p. 465.
- (217) OGLESBY AND EHRENFELD: Chem. Abstracts **22**, 1419 (1928).
- (218) OTTO: Ber. **23**, 1108-10 (1890).
- (219) PAAL AND SCHULZE: Ber. **36**, 2386-404 (1903).
- (220) PAAL AND STERN: Ber. **32**, 530-1 (1899).
- (221) PASCAL: Bull. soc. chim. [4] **5**, 1110-8 (1909).
- (222) PASCAL: Ann. chim. [8] **19**, 4-70 (1910).
- (223) PASCAL: Bull. soc. chim. [4] **11**, 111-21 (1912).
- (224) PAVLOVSKII: J. Russ. Phys. Chem. Soc. **43**, 214-8 (1911).
- (225) PERKIN: J. Chem. Soc. **47**, 801-55 (1885).
- (226) PERKIN: J. Chem. Soc. **59**, 786-97 (1891).
- (227) PERKIN: J. Chem. Soc. **65**, 402-32 (1894).
- (228) PERKIN AND DUPPA: Ann. **108**, 106-13 (1858).
- (229) PERKIN AND DUPPA: Chem. Soc. Quart. J. **11**, 22-30 (1859).
- (230) PERKIN AND DUPPA: Ann. **112**, 125-7 (1859).
- (231) PONZIO: Gazz. chim. ital. **37**, II, 41 (1907).
- (232) POPPE: Ber. **23**, 108-13 (1890).
- (233) PRESTON AND JONES: J. Chem. Soc. **101**, 1930-45 (1912).
- (234) PURVIS AND McCLELAND: J. Chem. Soc. **101**, 1810-23 (1912).
- (235) RADZISZEWSKI AND WISPEK: Ber. **15**, 1743-8 (1882); **18**, 1279-82 (1885).
- (236) RAMSPERGER AND WADDINGTON: J. Am. Chem. Soc. **55**, 214-20 (1933).
- (237) RANKEN AND NOBEL INDUSTRIES, LTD.: Chem. Abstracts **22**, 2421 (1928).
- (238) REINER: Ber. **14**, 1797-1802 (1881).
- (239) RICHARD: Compt. rend. **133**, 878-80 (1901).
- (240) RICHE: Compt. rend. **49**, 176-9 (1859).
- (241) RICHE: Ann. **112**, 321-6 (1859).
- (242) RUPE AND BUSOLT: Ber. **40**, 4537-40 (1907).
- (243) RUST: Ber. **30**, 2828-34 (1897).
- (244) SABANIEFF AND DWORKOWITCH: Ann. **216**, 279-86 (1883).
- (245) SABATIER AND MAILHE: Compt. rend. **169**, 758-61 (1919).
- (246) SCHERLING AND KAHLBAUM: Chem. Abstracts **22**, 3669 (1928).
- (247) SCHMIDT: Arch. Pharm. **236**, 334-43 (1898).
- (248) SCHOLL AND MATTHAIPOULOS: Ber. **29**, 1550-8 (1896).
- (249) SCHOLL AND SCHOEFFER: Ber. **34**, 870-81 (1901).
- (250) SCHRAMM: Ber. **18**, 606-9 (1885).
- (251) SCHRAMM: Ber. **18**, 1272-9 (1885).

- (252) SCHROETER: Ber. **37**, 1090-3 (1904).
- (253) SCHROETER: Ber. **40**, 1589-1604 (1907).
- (254) SELL AND LIPPMAN: J. prakt. Chem. [1] **99**, 432 (1866).
- (255) SELL AND LIPPMAN: Z. Chem. **9**, 724 (1866).
- (256) SELL AND SALZMANN: Ber. **7**, 496-7 (1874).
- (257) SEN: Quart. J. Indian Chem. Soc. **1**, 1-8 (1924).
- (258) SENTER: J. Chem. Soc. **99**, 95-103 (1911).
- (259) SHOESMITH: J. Chem. Soc. **123**, 2828-30 (1923).
- (260) SHOESMITH, HETHERINGTON, AND SLATER: J. Chem. Soc. **125**, 1312-9 (1924).
- (261) SHOESMITH AND RUBLI: J. Chem. Soc. **1927**, 3098-3106.
- (262) SHOESMITH AND SLATER: J. Chem. Soc. **125**, 2278-83 (1924).
- (263) SHUFFLEBOTHAM: Report No. 8, Chemical Warfare Medical Committee.
- (264) SIMONCINI: Gazz. chim. ital. **31**, II, 497 (1901).
- (265) SIMPSON: Ann. **113**, 115-25 (1860).
- (266) SLATOR: J. Chem. Soc. **87**, 481-500 (1905).
- (267) SLATOR AND TWISS: J. Chem. Soc. **95**, 93-103 (1909).
- (268) SLIMMER: Ber. **36**, 289-95 (1903).
- (269) Société Chimique des Usines du Rhône: Chem. Abstracts **12**, 910 (1918).
- (270) SOKOLOWSKY: J. Russ. Phys. Chem. Soc. **8**, 330 (1875).
- (271) SOKOLOWSKY: Ber. **9**, 1687 (1876).
- (272) SOMMELET: Compt. rend. **157**, 852-4 (1913).
- (273) SPREK: Monatsh. **11**, 429-32 (1890).
- (274) SPRUNG: J. Am. Chem. Soc. **52**, 1640-9 (1930).
- (275) STAEDEL: Ber. **9**, 562-3 (1876).
- (276) STAEDEL: Ber. **10**, 1830-41 (1877).
- (277) STAEDEL AND KLEINSCHMIDT: Ber. **13**, 836-8 (1880).
- (278) STAEDEL AND RÜGHEIMER: Ber. **9**, 563-4 (1876).
- (279) STAEDEL AND RÜGHEIMER: Ber. **9**, 1758-61 (1876).
- (280) STAUDINGER AND MÄCHLING: Ber. **49**, 1973-7 (1916).
- (281) STEINKOPF, MIEG, AND HEROLD: Ber. **53**, 1144-8 (1920).
- (282) STOERMER AND DZIMSKI: Ber. **28**, 2220-7 (1895).
- (283) STOLLE: Ber. **41**, 954-5 (1908).
- (284) STOLTZENBERG: Chemische Fabrik. Hamburg (1930).
- (285) SWARTS: Chem. Zentr. **1903**, I, 14.
- (286) SZPER: Bull. soc. chim. **51**, 653-6 (1932).
- (287) TCHERNIAC: Ber. **25**, 2629-32 (1892).
- (288) TCHERNIAC: J. Chem. Soc. **115**, 1071-90 (1919).
- (289) TCHERNIAC AND NORTON: Compt. rend. **96**, 494-7 (1883).
- (290) TCHERNIAC AND NORTON: Ber. **16**, 345-8 (1883).
- (291) THOMAS: J. Chem. Soc. **103**, 594-604 (1913).
- (292) TIEMANN: Ber. **31**, 808-66 (1898).
- (293) TIFFENEAU: Compt. rend. **134**, 774-5 (1902).
- (294) TIFFENEAU: Compt. rend. **137**, 989-91 (1903).
- (295) TIFFENEAU: Compt. rend. **138**, 985-7 (1904).
- (296) TIFFENEAU: Ann. chim. [8] **10**, 145-98 (1907).
- (297) TIFFENEAU: Ann. chim. [8] **10**, 322-78 (1907).
- (298) TITLEY: J. Chem. Soc. **1926**, 508-19.
- (299) TSCHITSCHIBABIN: J. prakt. Chem. [2] **73**, 326-36 (1906).
- (300) TUTIN: J. Chem. Soc. **97**, 2495-2524 (1910).
- (301) ULRICH AND ADAMS: J. Am. Chem. Soc. **43**, 660-7 (1921).

- (302) VAN DER LAAN: *Rec. trav. chim.* **26**, 1-54 (1906).
- (303) VAN REYMEYNT: *Bull. acad. roy. méd. Belg.*, pp. 724-44 (1900).
- (304) VEDDER: *The Medical Aspects of Chemical Warfare*. The Williams & Wilkins Co., Baltimore (1925).
- (305) WACHTEL: *Z. exptl. Path. Therap.* **21**, 1-18 (1920).
- (306) WALDEN: *Ber.* **35**, 2018-31 (1902).
- (307) WALLACH: *Ann.* **360**, 26-7 (1908).
- (308) WHEELER: *J. Am. Chem. Soc.* **51**, 3653-5 (1929).
- (309) WHEELER AND WALKER: *J. Am. Chem. Soc.* **47**, 2792-6 (1925).
- (310) WIDMAN: *Ber.* **49**, 478 (1916).
- (311) WIDMAN: *Ber.* **51**, 533-4 (1918).
- (312) WIDMAN AND ALMSTRÖM: *Ann.* **400**, 86-130 (1913).
- (313) ZABOEV: *Zhur. Obshchei Khim.* **1**, 143-9 (1931).
- (314) ZAHN: *Physik. Z.* **33**, 686-7 (1932).
- (315) ZELTNER AND TARASSOW: *Ber.* **43**, 941-5 (1910).

SEMIQUINONES, THE INTERMEDIATE STEPS OF REVERSIBLE ORGANIC OXIDATION-REDUCTION

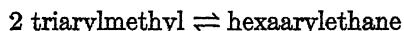
LEONOR MICHAELIS

Laboratories of The Rockefeller Institute for Medical Research, New York City

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Reversible oxidation-reduction systems may be classified in two groups, according to what we call the electron number, that is to say, whether the oxidized form differs from the reduced by one electron (or hydrogen atom) or by two. We also speak of univalent and bivalent oxidation. Cases of univalent oxidation are rather common in inorganic compounds, such as in ferric-ferrous or cupric-cuprous systems, either in the form of simple metal ions or complex compounds. But they are rare, and in fact, have not been known at all until recently, in organic chemistry. Authors to whom we owe very outstanding contributions to our knowledge of reversible oxidation-reduction processes (6) are so much impressed by the lack of univalent oxidations in organic compounds that they correlate the simultaneous loss of two electrons with the trend of electrons towards arrangement in pairs, which is the main principle of Langmuir's and G. N. Lewis' theory of the chemical bond. Such a view, however, can be maintained only in a restricted sense. The situation is rather as follows.

In the metals of the transition series of the periodic systems, as iron and cobalt, a univalent oxidation occurs whenever two levels of oxidation, differing by one electron, are capable of existence. Thus ferrous ions contain one more electron than ferric ions. However, disregarding some exceptional cases, organic compounds possess only atoms with fixed valence numbers. These exceptional cases, such as triarylmethyl with tervalent carbon, or diarylnitride with bivalent nitrogen, are considered as unsaturated compounds—radicals capable of existence only under special conditions depending on the chemical nature of the particular aryl—and they exhibit a strong tendency toward abolishing the unsaturated state by dimerization, as follows



although in some particular cases this latter tendency may be weak. The customary way of studying reversible organic oxidation-reduction systems in an aqueous solvent did not seem to offer any chance of encountering a

radical of this kind. As a rule, the oxidized form has a quinoid structure, and the reduced form has the corresponding benzenoid structure as encountered in the leuco dyes. The univalent oxidation of the benzenoid form would lead to a radical with a structure intermediate between the quinoid and the benzenoid form.

As a matter of fact, however, such intermediate forms of oxidation had been known for a very long time. Their simplest representative is quinhydrone. But so great was the aversion to thinking of them as unsaturated radicals, that this substance was taken as a molecular compound of quinone and hydroquinone. It does not seem appropriate to dwell on the many tentative formulas ascribed to quinhydrone. We may just picture Willstätter's (62) formula. He assumes that a residual valence of oxygen holds together one molecule of quinone with one of hydroquinone. In addition, he assumes that no static formula truly depicts the constitution of quinhydrone, but that an oscillation of the bonds takes place so that the reduced half and the oxidized half of the molecule take turns in rapid succession. For this reason he termed these compounds meriquinones, which means that, in a time average, the state of oxidation is evenly distributed ($\mu\acute{\epsilon}\rho\omicron\varsigma$ = part) among the two halves. As regards the even distribution, we shall share his point of view. As regards the molecular size, we shall be compelled to disagree.¹ Willstätter's point of view appeared to be even more justified by the fact that such molecular compounds, between two different molecules, one of a higher oxidation level than the other, do exist, even in ratios other than 1:1, e.g., a compound of one molecule of quinone and two molecules of phenol, or five of quinone and two of *p*-phenylenediamine (Schlenk (46)). In fact, it is very suggestive, that by analogy with a compound consisting of 1 quinone + 2 phenol, a compound of 1 quinone + 1 hydroquinone should also be capable of existence, and that quinhydrone is this compound. Such an assumption would be corroborated by a determination of the molecular weight. No method was available to decide as to the molecular size of quinhydrone. So Willstätter's interpretation of the meriquinoid substances as encountered in many groups of organic dyestuffs was in general accepted. To prove this statement let it suffice to quote, as examples, Schlenk's (46) formula of the meriquinone obtained by partial oxidation of dichlorotolidine or Dimroth's formula for the meriquinone obtained by partial reduction of γ,γ' -dipyridyl.

The first suspicion as to the correctness of the bimolecular structure was uttered by Hantzsch (23), although he had no cogent evidence. He observed that the green compounds obtained by partial reduction either of

¹ Recently Willstätter, in a paper published with Haber (22), has abandoned his original bimolecular formula.

N-methylphenazonium iodide, or of phenazine, showed two bands in the ultra-violet, a phenomenon which is observed neither in the fully reduced nor in the fully oxidized form, and is absent also in compounds of a doubtlessly bimolecular meriquinoid structure. He failed, however, to find any representative of this group suitable for a determination of the molecular weight by the methods available. Later, E. Weitz (59) succeeded in determining the molecular weight of some compounds of this group by the boiling point method in organic solvents. He worked on the meriquinoid compounds obtained by mixing equivalent amounts of dibenzyl- γ,γ' -dipyridylum dichloride with dibenzyl- γ,γ' -dipyridylum. The latter substance can be considered, as he showed (55), as a free ammonium radical, or better, a double radical, because it contains the ammonium group twice. In mixing these two compounds a deep violet dyestuff is developed, which can be prepared in crystalline form and may be considered as a meriquinoid compound. The problem was whether the molecular weight of this substance is that of a compound or condensation product of the two parent substances, or whether it has the same molecular size as either of the parent substances. The analysis showed that it contains one chlorine atom to two nitrogen atoms; this would agree with either assumption. He determined the boiling point of this substance in water-free methanol in an atmosphere of carbon dioxide free from oxygen. For this purpose he elaborated a special technique of the boiling point method for oxygen-sensitive substances and obtained a molecular weight, corroborated by the good agreement of a very large number of single experiments, of 197 as an average from experiments with solutions more dilute than $M/16$ and 215 from experiments with concentrations greater than $M/16$. The molecular weight of the substance if it be monomolecular would be 373. Assuming 100 per cent dissociation of the chloride ion, the apparent molecular weight should be 187, which agrees very well with the experiment. This result was taken as evidence that the monomolecular radical formula was proven. Assuming the dimolecular formula and complete dissociation of the two chloride ions, one should obtain an apparent molecular weight of 235. Yet it is known how uncertain the interpretation of this method is when applied to an electrolyte. In the same paper Weitz carries out a determination of the molecular weight of dibenzylidipyridinium dichloride (the colorless oxidation product of the above radical) having a molecular weight of 409. Again, assuming total dissociation of the chlorine one should expect an apparent molecular weight of 136. However, he finds in three experiments 253, 243, and 283, which necessitates the assumption that one of the two chlorine atoms is not ionized at all and the other only in part. Such an observation is liable to arouse some doubt as to the general applicability of the method to organic electrolytes. One may recall the fact that later

Wrede (64, 65) was also misled by the freezing point method of another dye, pyocyanine, to which he ascribed a molecular weight double what we think is the real one. Although Weitz may have been fortunate in the above case of the dye radical, a confirmation by another method is desirable. Such a method is the potentiometric oxidative or reductive titration.

THE APPLICATION OF THE POTENTIOMETRIC METHOD TO THE PROBLEM

This method was first applied to the study of merquinoid compounds by W. Mansfield Clark, B. Cohen, and W. Gibbs (4). They happened to work with a group of merquinoid compounds of a very labile nature, principally with those of the benzidine compounds. The potentials obtained during the titration showed rapid drifts, so that a real insight into the mechanism of the process could not be obtained. Guided by the current ideas it was quite natural that they did not doubt Willstätter's bimolecular formula. They developed a complete theory for the potential curve obtained on the basis of their assumptions, but had no opportunity to test the theory with their experimental material on account of the drifts of potential. The first case in which a compound of this type, perfectly stable even in aqueous solution, was encountered, is that of pyocyanine, first described by Friedheim and Michaelis (21), and only a little later and independently by Elema (10). Neither the first paper on this subject by Friedheim and Michaelis, nor that by Elema, led to a complete understanding, as the theory presently to be developed had not yet been worked out. It is of no use to dwell on a detailed comment on the preliminary results then obtained. We had better start with the complete theory which very soon after that was developed by these authors (39, 11, 12).

The case of two-step oxidation has many analogies to the two-step dissociation of dibasic acids. So the question may arise as to why the complete theory of such a two-step process has not been previously developed, at least for the case of acidic dissociation. Now, in the case of a two-step dissociation, the titration curve plotted against pH will, in general, show two successive levels separated from each other by a jump. The height of this jump will depend on the ratio of the two dissociation constants of the dibasic acid. The smaller this ratio, the smaller the jump. The smallest ratio which theoretically can occur is 4:1. This is often called the "statistical ratio"; a smaller ratio has been shown to be impossible for statistical reasons. In practice the ratio is always much greater, and there is scarcely a case known where this ratio is smaller than 20:1. For this reason the jump between the two halves of the curve is always so large that any overlapping of the two curves is negligible. The two steps of dissociation can be treated as two simple dissociation curves in succession. In the case of two-step oxidation-reduction we have to deal also with two char-

acteristic constants, to be defined later on, which are analogous to the two dissociation constants, but for these constants any ratio may occur, even smaller than 4:1, and even a ratio smaller than 1:1. In such a case the two halves of the curve are no longer separated by a jump, but overlap. For this reason the theory has to be developed in a more general way, including also the case of overlapping. The theory will be developed here, first for the simpler case with distinct steps, then for the general case including the overlapping.

A. The case of distinctly separate steps

Suppose we have a substance R which can be reversibly oxidized in two successive steps, each involving the loss of one electron. The completely oxidized form may be called T, so that its relation to R is expressed by



where ϵ is the electron. If the intermediate form differs from R and from T only by an electron without change of molecular size, the intermediate form may be called a semiquinone, S, and the following relations hold.²



If, however, the intermediate form is a molecular compound, it may be called a meriquinone, M. We restrict ourselves for the time being to the simplest case, that M is a compound of one molecule R and one molecule T. It is easy to see that the assumption of other stoichiometrical proportions, say R:T = 1:2, will not alter anything essential in the corollaries to follow. Then the following relations hold:



As all reactions are supposed to be reversible, the intermediary form must be in equilibrium with the two others, and it will be able to undergo a self-oxidation-reduction, or a dismutation or disproportionation, or a kind of Cannizzaro reaction. On applying small letters for concentrations, this equilibrium will be determined in the case of a semiquinone by

$$k \cdot r \cdot t = s^2 \quad (4a)$$

where k may be termed the formation constant of the semiquinone, or

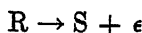
² The symbols used are in alphabetical order: R (reduced), S (semiquinone), T (totally oxidized).

$1/k$ the dismutation constant. If the intermediate form is a meriquinone, the equation for equilibrium will read

$$k' \cdot r \cdot t = m \quad (4b)$$

When a solution containing only R is titrated with an oxidant, the magnitude of k or k' will determine how much of S or M can be formed *in maximo* during the titration. If k is very small the two steps will greatly overlap. If this constant is very large, at the beginning of the oxidative titration only S or M will be formed, and T will arise only after practically all R has been converted into S, or M. In such a case the two steps of oxidation are said to be distinctly separated.

In this case each of the two steps of oxidation can be treated separately, as there is practically no overlapping. In the first half of the titration the chemical process is, for the case of a semiquinone:



and the oxidation-reduction potential is

$$E = E_1 + \frac{RT}{F} \ln \frac{s}{r} \quad (5a)$$

where the constant E_1 may be called the normal potential of the R-S system. For the case of a meriquinone, the potential is

$$E = E_1 + \frac{RT}{2F} \ln \frac{m}{r^2} \quad (5b)$$

Analogous equations may be written for the second step of oxidation, in which the normal potential E_2 necessarily is much more positive than E_1 . We shall develop the details only for the first step, as the second step is a repetition of the first; a complete repetition for the case of a semiquinone, and a kind of antisymmetrical repetition for the case of a meriquinone. On comparing equations 5a and 5b, it can be seen that for a semiquinone the potential depends only on the ratio $r:s$, but for a meriquinone also on the absolute amount of the substances. We may rewrite equation 5b in a more suitable form. Let v be the volume of the solution, (R) the absolute amount of R in moles, then we obtain

$$E = E'_1 + \frac{RT}{2F} \ln \frac{m}{r} - \frac{RT}{2F} \ln \frac{(R)}{v}$$

This equation shows that the titration curve, i.e., potentials plotted against the amounts of added oxidant, is distorted as compared with equation 5a. The differentiation with respect to v gives

$$\frac{dE}{dv} = \frac{RT}{2F} \cdot \frac{1}{v}$$

or, all variables besides v being kept constant, $\Delta E = 0.03 \log \frac{v_1}{v_2}$. So E depends on v , whereas in the case of a semiquinone the potential is independent of the volume. Thus, in the case of a meriquinone, the potential depends on the volume in which a given amount of substance R is dissolved. On varying this initial volume, one obtains a family of titration curves parallel to each other, the distance amounting to 0.03 volt when the volumes are varied in a ratio 1:10. So the following criteria can be established:

For a semiquinone:

1. The titration curve is symmetrically arranged around its middle ordinate.³
2. The shape of the curve is that of an ordinary one-electron system.
3. The curve of the potentials as plotted against per cent of oxidation is independent of the volume.

For a meriquinone:

1. The titration curve is not symmetrical about its middle ordinate, but steeper in the first half than in the second.⁴
2. The shape of the curve is somewhat between that of a one-electron system and a two-electron system; one half (the steeper one) approaching somewhat that of a one-electron system, the other being more similar to that of a two-electron system.
3. The curve of the potentials as plotted against per cent of oxidation depends on the volume in which the initial amount of the substance was dissolved. It is shifted toward the positive side by 0.03 volt when the volume is varied in the ratio 1:10.

³ More precisely: Draw an x-axis and a y-axis intersecting in the midpoint of the titration curve. When the second half of the curve is now mirrored in the x-axis (dotted curve), this is a mirror-image of the first half in the y-axis.

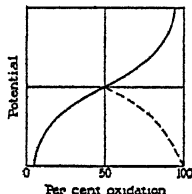


FIG. 1

⁴ If the titration concerns the second step of oxidation, the first half is flatter than the second.

When these criteria are applied to an experiment as plotted in figure 2 and described in the legend of this figure, all criteria for a semiquinone and none for a meriquinone are fulfilled. As yet, no case has been found where the result was different from this one.

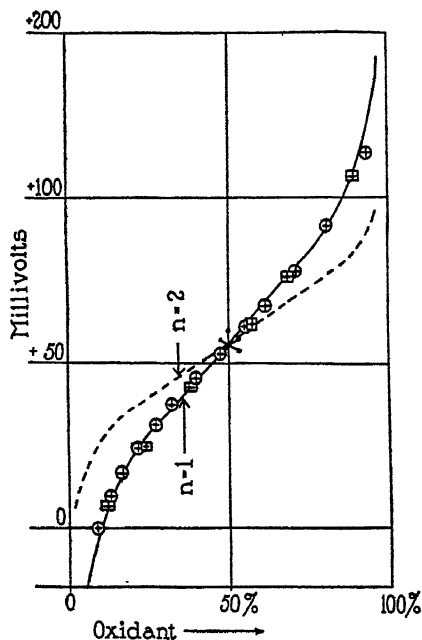


FIG. 2. Showing the independence of the potential of the concentration of the dye. α -Oxyphenazine at pH 1.382 (solution 0.05 *M* for HCl and 0.1 *M* for KCl). Only the first step of the oxidation of the leuco dye is plotted. The abscissa indicates the amount of quinone, expressed in per cents of that amount which completes the first step of oxidation; the ordinates are potentials. The first experiment is represented by the circles. After finishing this experiment, the whole solution was diluted with the above acid mixture (containing no dye) to a threefold volume, the dye re-reduced by hydrogen and palladium, the hydrogen expelled, and the titration with quinone was repeated. It furnished the points marked with squares. The drawn out line is the one calculated for an oxidation with the electron number 1; the dash line the one calculated for the electron number 2.

B. The general case, including that with overlapping potentials

In most cases the separation of the two steps becomes less distinct as the pH increases, until finally the overlapping of the two steps becomes complete. The explanation of this fact will be dealt with later on. When, now, for a particular dye the decision for a semiquinone at a sufficiently low pH has been made, we assume that this decision can be maintained also for higher pH, where the above criteria no longer can be applied with-

out modification which could only very laboriously be obtained. This assumption is justified by the fact that no recognizable change, especially with regard to the color, of the intermediate form appears on changing pH. To be sure when the overlapping is considerable, the pure color of the semiquinone will never appear, but only mixtures of it with colors of the other forms. Yet the absorption of the semiquinone can be recognized even in the mixture, owing to the color intensity of most of the semiquinones. So there is no reason to assume that the intermediate form has a different structure according to whether the separation of the steps is more or less complete. The problem now arises as to the analysis of complete titration curves including the cases of overlapping. This problem has been solved in two ways, by Elema and by Michaelis. The formulas arrived at, at the first glance, look so different that their agreement was not recognized at first. Elema, however, succeeded in proving, very ingeniously, that the one formulation is the somewhat disguised equivalent of the other. The advantage of Elema's formulation will be shown later. The other seems the easier one from the standpoint of presentation and is given in what follows.

When overlapping takes place at any point of the titration there will be a mixture of R, S, and T. The whole system being in equilibrium, the oxidation-reduction potential can be expressed in three different ways, according to the three partial oxidation-reduction systems in solution, viz. the system R-T, the system R-S, and the system S-T. The potential, then, can be formulated in any of these three ways:

$$(1) \quad E = E_m + \frac{RT}{2F} \ln \frac{t}{r} \quad (6a)$$

$$(2) \quad E = E_1 + \frac{RT}{F} \ln \frac{s}{r} \quad (6b)$$

$$(3) \quad E = E_2 + \frac{RT}{F} \ln \frac{t}{s} \quad (6c)$$

Notice that the factor 2 appears only in the first equation, as only the R-T system is a two-electron system. E_1 may be called the normal potential of the first step; E_2 that of the second step; and E_m the "mean normal potential." These three normal potentials are not independent of each other. It can easily be inferred from these three equations that E_m is the arithmetic mean of E_1 and E_2 , or

$$E_m = \frac{E_1 + E_2}{2} \quad (7)$$

The relation between k and the normal potentials can be recognized by dividing equation 6c by equation 6b and referring to equation 4a. One obtains

$$\frac{RT}{F} \ln k = E_2 - E_1$$

or, at 30°C.,

$$\log k = \frac{E_2 - E_1}{0.0601} \quad (8)$$

In order to evaluate these three equations (6a, 6b, 6c) we have to express r , s , and t in terms of total concentration, a , of the dye, and of the amount x of added oxidant. We have always

$$r + s + t = a \quad (9)$$

Further, after adding x univalent equivalents of oxidant, we have:

$$s + 2t = x \quad (10)$$

x is measured then in terms of equivalents of oxidation for one step, so that at the end point of the titration $x = 2a$. The solution for the three unknowns, r , s , t , requires a third independent equation which is the above mentioned (4a)

$$k \cdot r \cdot t = s^2 \quad (4a)$$

The solution of these three equations (9, 10, 4a) for r , s , and t , is

$$r = a \left(1 + \frac{p}{2} \right) - \frac{x}{2} \mp \frac{1}{2} \sqrt{Y} \quad (11)$$

$$s = -a \cdot p \pm \sqrt{Y} \quad (12)$$

$$t = a \cdot \frac{p}{2} + \frac{x}{2} \mp \sqrt{Y} \quad (13)$$

where

$$p = \frac{k}{4 - k} \quad (14)$$

and

$$Y = a^2 p^2 + 2apx - px^2 \quad (14a)$$

So the formation constant k appears only in the form $\frac{k}{4 - k}$, which term changes in sign according to whether $k \geq 4$. As to the signs before the square roots, the upper sign should be used when $k < 4$, and vice versa.

For the particular case $k = 4$, the general solution becomes indefinite, but a singular solution can be obtained either by interpolation, or by directly putting $k = 4$ in equation 4a. In this case the solution is

$$r = \frac{(2a - x)^2}{4a} \quad (15a)$$

$$s = \frac{x(2a - x)}{2a} \quad (15b)$$

$$t = \frac{x^2}{4a} \quad (15c)$$

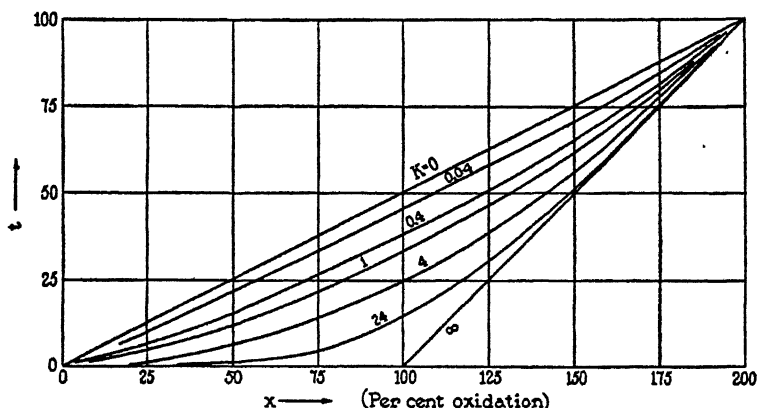


FIG. 3. t , the totally oxidized form (or quinoid, or holoquinoid form) in per cents of the total amount of the dye plotted against per cent of oxidation. When the scale of the abscissa is reversed, it is r , the reduced form plotted against per cent of oxidation.

These latter three functions are parabolic, whereas the others (11, 12, 13) are hyperbolic and consist, purely mathematically, of two branches of which only one has a physical significance, namely, to cover the range from $x = 0$ to $x = 2a$. So it is evident that on varying k , the value $k = 4$ will have some special significance, as will be shown in fact. The rather laborious evaluations of these functions for various values of k are plotted in figures 3 and 4. Figure 3 shows the amount of r , as a percentage of the total amount of the dye, plotted against per cent of oxidation, the whole oxidation being taken as 200 per cent (or, $a = 100$). When the abscissa is reversed according to the legend of the graph, we obtain the percentage of t . Figure 4 shows the percentage of s plotted against percentage of oxidation.

The values thus obtained for r , s , t can now be put in equations 6a, 6b, 6c in order to obtain the expressions for the potentials. Figure 5 is the result of such a calculation. As only differences of potentials are essential for the shape of the curves, the potential in the midpoint of titration ($x = 100$) for each curve has been arbitrarily taken equal to 0.

All that follows depends on a full understanding of this family of curves, which is to be discussed now in detail. Looking first at the curve $k = 100$ we recognize two steps, each one matching an ordinary titration curve of a one-electron system. The curve shows the value E_1 , the normal potential of the first step, in the midpoint of the first half of the curve, and the value E_2 at the midpoint of the second half. These points are marked by circles. As k becomes greater the jump from the first step to the second is higher,

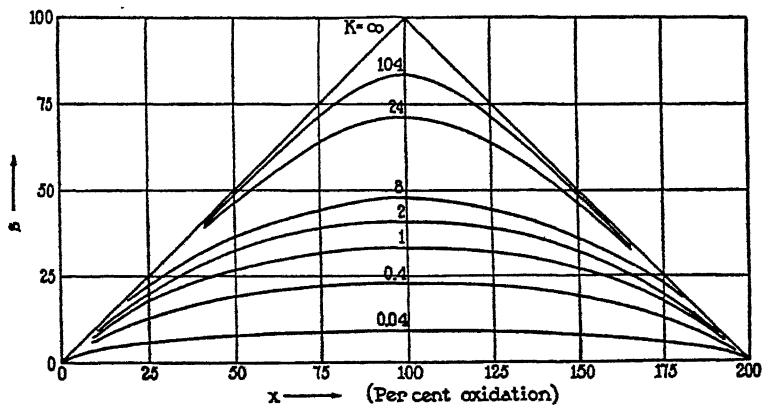


FIG. 4. s , the semiquinoid or intermediary form in per cents of the total amount of the dye plotted against per cent of oxidation.

or $E_2 - E_1$ becomes greater. As k becomes smaller, not only does this jump become smaller but also the circles are more and more shifted toward the middle, until for $k = 1$ all three circles coincide in the center of the figure. The curve $k = 4$ will be expected to be singular in behavior. This is shown by the fact that the two points of inflection, very distinct for high values of k , become less marked with decreasing k and completely vanish at $k = 4$. Here the curve as a whole has precisely the shape of an ordinary one-electron system. Neither the two-step nature of such a system nor the bivalent character of the oxidation could be recognized experimentally were there not the twofold change of color during the titration. Such a case is, for example, realized for pyocyanine at pH 5.0. When k becomes < 4 , the curve becomes flatter until finally, at $k = 0$, it coincides with an ordinary two-electron system as represented by most reversible

quinoid dyestuffs. The circles indicating E_1 and E_2 are drawn only for curves with $k > 1$. At $k = 1$, E_1 and E_2 coincide with E_m , which lies always in the midpoint of each curve. For curves with $k < 1$ no circles have been drawn lest the diagram be crowded. For such curves, in contrast to the others, the circle for E_1 lies on the right-hand side of the center, and the one for E_2 on the left-hand side. This fact may be accounted for by saying that if $k < 1$, the oxidation of the reduced form leads more easily to the fully oxidized form than to the intermediary form, in the same way as,

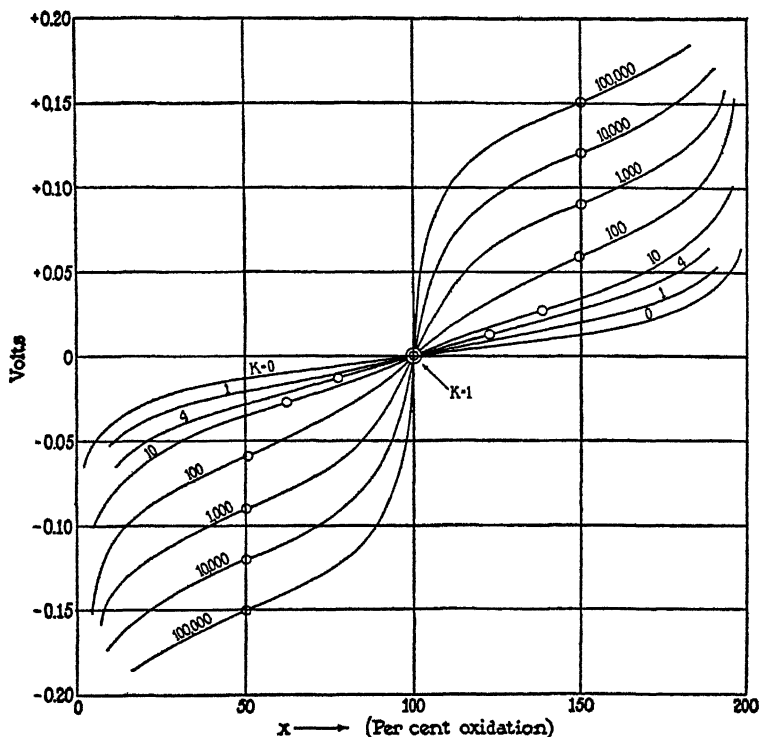


FIG. 5. The potential (in volts) plotted against per cent of oxidation

generally, the oxidation of copper leads more easily to the cupric state than the cuprous.⁵ Finally, when $k = 0$, the intermediate form is not developed at all, and we have the situation of an ordinary quinoid dye having no semiquinone form at all.

⁵ This case is not, however, quite comparable in every respect to the others, as the system—metallic copper plus a solution of copper salts—is a two-phase system, whereas we have to deal here with a homogeneous system.

This is the right place to look back at figure 4. The amount of semiquinone formed *in maximo* during the titration is always at the midpoint (100 per cent in figure 5). But even when k is as small as 1, in which case, according to the above reasoning, the normal potential of the lower step equals the one of the higher step, as much as 33.3 per cent of the dye is present as semiquinone at the midpoint of the titration.

DEPENDENCE OF k ON pH

To adapt the theory to actual conditions one has to consider that the equations 9 and 10 do not take into account that all these substances are acids (or bases), and that the difference between the oxidized and the reduced state may be not only an electron, but a full hydrogen atom. Each kind of molecule concerned may be present in several states of acidic dissociation. Equations 9 and 10 hold even then, provided we understand by r the total concentration of the reduced form in all its states of electrolytic dissociation, and the same holds for s and t . But equation 4a has to be modified. This equation holds only if we mean by r , s , t , just such forms of the three kinds of molecules as differ from each other only by electrons, not by full hydrogen atoms. When we pick out of all possible states of dissociation three particular ones r' , s' , t' , which differ from each other only by electrons, equation 4a is valid. Now according to the mass law

$$r' = f_1(r, k_1, k_2, \dots, \text{pH})$$

where $k_1, k_2, \dots$ are the various successive dissociation constants of R, and f_1 is the symbol of some function the form of which is irrelevant for the time being. Analogous equations hold for s' and t' . These functions may be symbolized by f_2 and f_3 . Equation 4a then reads

$$r \cdot t \cdot k \cdot \frac{f_1 \cdot f_3}{f_2^2} = s^2 \quad (16)$$

and taking

$$k \cdot \frac{f_1 \cdot f_3}{f_2^2} = K$$

the equation 16 has the same form as equation 4a, the difference being only that the constant k , which is independent of pH, is replaced by the "effective formation constant" K , which depends on pH.

For an individual dye K will vary with pH, and for this reason the shape of the titration curve of a dye may vary according to pH throughout all the possibilities as shown in figure 5. This is the explanation for the previously and preliminarily mentioned fact that a distinct separation of the two steps may be accomplished by working at a suitable pH. So, all the

equations 11, 12, 13, 14, and 14a hold good, provided we apply K instead of k . We may designate k as the true formation constant of the semiquinone and K as the effective constant.

ADAPTATION OF THE THEORY FOR PRACTICAL APPLICATION

Heretofore we have started from a given value for K , taking it as the independent variable, and derived from it the shape of the titration curve. In practice, we have to deal with the reverse process. The experiment furnishes the titration curve, and we have to derive from it the value of K and of the three normal potentials. It is obvious that a strict and complete analysis of an experimentally obtained curve is not feasible on account of its complicated nature. However, since the various curves of figure 5 do not intersect except in the common midpoint, it is possible to match any experimentally obtained curve to a particular one of this family, and so to arrive at the value of K pertaining to it. To simplify this procedure, two methods have been recommended.

A. Michaelis' method

Let us define the magnitude E_i , the "index potential", by

$$E_i = E_{\frac{1}{2}} - E_{\frac{1}{4}} \quad (17)$$

where $E_{\frac{1}{2}}$ signifies the potential at the midpoint of the curve, at 50 per cent of the total oxidation (which is 100 per cent in the graph, figure 5), and $E_{\frac{1}{4}}$ is the potential at 25 per cent of the total oxidation (50 per cent in figure 5). On account of symmetry $E_i = E_{\frac{1}{2}} - E_{\frac{1}{4}} = E_{\frac{3}{4}} - E_{\frac{1}{2}}$. The occurrence of this symmetry in the experimental curve is a necessary criterion that the curve belongs to this family. Now it can be seen from figure 5 that K can be correlated with E_i . So we may set up an interpolation table from which for each value of E_i the corresponding value of K can be read. This is given in table 1, holding for a temperature of 30°C. It was first evaluated by the writer by means of graphical interpolation. A sufficient number of values were computed according to formulas 6 and 11 to 13, taking such values of K as to render the algebra easy, and the intermediate values were graphically interpolated. Later, Elema discovered a method of direct and strict calculation of any value of K from E_i . He arrived at the equation

$$K = \left(a - \frac{3}{a} \right)^2 \quad (18)$$

where $a = 10^{\frac{E_i}{0.0601}}$. This equation was derived by Elema from equation 21 of the next section. By this method the interpolation values formerly

obtained could be checked and were found practically in agreement with the calculated, except for very slight errors, amounting at the worst to a few tenths of a millivolt, in the range from $K = 0$ to $K = 1$. This range is most sensitive to slight errors in the interpolation method. No practical consequence ensues from Elema's correction. In any case, the table given above has been corrected according to Elema's recalculation. We read from this table the value of $\log K$ correlated with any value of

TABLE 1
Interpolation table

$\log K$	$0.0601 \log K = E_2 - E_1$	E_2
		<i>volts</i>
$-\infty$		0.0143
-3	-0.1803	0.0146
-2	-0.1202	0.0151
-1.5	-0.0901	0.0157
-1.3	-0.0781	0.0160
-1.0	-0.0601	0.0167
-0.8	-0.0481	0.0174
-0.6	-0.0361	0.0181
-0.4	-0.0240	0.0191
-0.2	-0.0120	0.0203
0	0	0.0218
+0.2	+0.0120	0.0237
+0.4	+0.0240	0.0258
+0.6	+0.0361	0.0286
+0.8	+0.0481	0.0320
1.0	+0.0601	0.0362
1.2	+0.0721	0.0404
1.4	+0.0841	0.0448
1.6	+0.0962	0.0494
1.8	+0.1082	0.0546
2.0	+0.1202	0.0601

Whenever $\log K > 2$, then $E_2 = 0.03005 \log K$.

E_1 . Experimentally we obtain E_1 . From this, the table gives K , and hence $E_1 - E_2$, which is correlated with K in this way (compare formula 8)

$$E_1 - E_2 = 0.06 \log K \quad (8a)$$

Besides, the experiment gives E_m , which is the potential at 50 per cent of the total oxidation. Now according to formula 7

$$E_m = \frac{E_1 + E_2}{2}$$

Herewith all data are available to arrive at E_1 and E_2 . Having E_m , E_1 , E_2 , K , the problem is solved as to how to derive the characteristics of the dye, valid at the pH of the experiment, from the shape of the titration curve.

B. Elema's method

The middle part of any titration curve of this family is approximately a straight line, the slope of which will be correlated with K . The slope of the tangent at 50 per cent of the total oxidation is easily determined graphically. This tangent intersects the ordinate at 100 per cent of the total oxidation at a point which differs from the value of the ordinate at 50 per cent of the total oxidation. This difference can be determined graphically. Let it be v volts. Then, at 30°C.

$$K = (76.63v - 2)^2 \quad (19)$$

How to arrive at this formula will be mentioned in the next section. This equation permits of direct numerical evaluation of K for any value of v .

REVIEW OF SOME FURTHER MATHEMATICAL DETAILS

Although it does not seem appropriate to enter into the mathematical details of the theory more than necessary for practical application, some of the formulations should be at least briefly mentioned. The reason why it is desirable to have formulas of another type is this: All the above formulas are ambiguous with respect to the sign before the square root. The range of x of physical significance is only that between $x = 0$ and $x = 2a$, and so the problem arises whether these functions might be put into such a form that, at least within this range, no change of sign takes place. Secondly the foregoing formulas are of such a nature that for the case $K = 4$ a special formula must be used. So the problem also arises whether some formula may be found which can be applied generally for any value of K . As regards the first problem it cannot be solved for the formulas 11, 12, and 13 for r , s , t , but it is possible for the formula for E . Elema developed a formula fulfilling the first condition that it involve no change of sign:

$$E = E_m - \frac{RT}{F2} \ln \frac{KT_r - KT_o - 8T_r + \sqrt{(KT_r - KT_o - 8T_r)^2 + 16(K-4)T_r^2}}{KT_o - KT_r - 8T_o + \sqrt{(KT_o - KT_r - 8T_o)^2 + 16(K-4)T_o^2}}$$

Here T_r signifies the "total amount of the reductant", T_o the "total amount of the oxidant." These definitions may be easily misunderstood. A more precise definition is this:

$$T_r = \frac{1}{2}s + r$$

$$T_o = \frac{1}{2}s + t$$

s , r , and t having the same significance as in the above formulas 11, 12, and 13. Later the same author developed another formula which fulfills both of the mentioned conveniences and has besides the advantage that it can be relatively easily differentiated and so be used for the calculation of the slope of the midpoint tangent and hence for the establishment of formula 19. This formula reads:

$$E = E_m - \frac{RT}{F} \ln \frac{4\alpha}{(1-2\alpha)\sqrt{K} + \sqrt{K(1-2\alpha)^2 + 16(1-\alpha)}} \quad (21)$$

where α is the "degree of reduction", or in terms of the previous definition,

$$\alpha = \frac{2a - x}{2a}$$

Herefrom an equation for the index potential E_i can be derived:

$$E_i = \frac{RT}{F} \log \frac{1}{2} (\sqrt{K} + \sqrt{K+12})$$

When this is solved for K , one obtains the above-mentioned equation (18). Besides Elema's formulas, I may present the following:⁶

$$E = E_m + \frac{RT}{2F} \ln \frac{\xi}{2-\xi} + \frac{RT}{2F} \ln \frac{\xi-1+\sqrt{(\xi-1)^2+4\kappa\xi(2-\xi)}}{1-\xi+\sqrt{(\xi-1)^2+4\kappa\xi(2-\xi)}} \quad (22)$$

Here $\xi = \frac{x}{a}$ and κ is the dismutation constant, $= \frac{1}{K}$. This formula also fulfills both the desired conveniences and furthermore illustrates the function in so far as its first logarithmic term is the same as for an ordinary bivalent oxidation without step formation, whereas the second logarithmic term takes care of the correction for step formation when $K > 0$.

⁶ For the derivation of Elema's formula we may refer to his original papers. To arrive at formula 22, proceed as follows. Divide equation 9 by a , put $\frac{x}{a} = \xi$, $\frac{r}{s} = \rho$, $\frac{t}{s} = \tau$. Modify equation 10 in the same way. Divide the thus modified equation 10 by the modified equation 9. Rewrite equation 4a in the form $\rho \cdot \tau = \kappa$. Solve these three equations for ρ and τ and put $E = E_m + \frac{RT}{2F} \ln \frac{\tau}{\rho}$. Equation 22 has resulted from suggestions which the writer owes to Professor Albert Einstein.

PRACTICAL APPLICATION OF THE METHOD TO TWO EXAMPLES AND
INTERPRETATION OF THE RESULT1. α -Oxyphenazine (41)

A series of titration curves at constant pH was made, over a wide range of pH, either by oxidizing the reduced form, or by reducing the oxidized form. The oxidized form is lemon-yellow between about pH 1 to 11; it

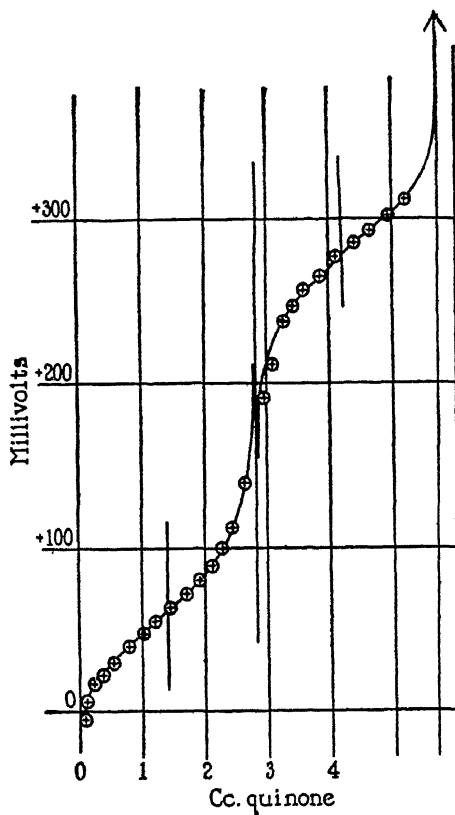


FIG. 6. Reduced α -oxyphenazine at pH 1.00 is titrated with quinone. Potentials referred to the normal hydrogen electrode.

turns red at pH < 1, and cherry-red at pH > 11. The semiquinoid form in all those pH ranges where it exists is green. The reduced form is almost colorless, very slightly yellow. One example of a titration is figure 6, another figure 7. Similar titration experiments were performed in a wide range of pH and the values of E_m , E_1 , and E_2 determined for each pH from these curves. The result of this set of experiments at varied pH is summarized in figure 8. Notice first of all the common point of intersection

of the three normal potentials E_m , E_1 , E_2 at pH 3.2. Here $E_m = E_1 = E_2$ and therefore $K = 1$, and the maximum amount of semiquinone that can exist beside the other forms is 33.3 per cent of the total dye. This occurs when half the amount of oxidant necessary for complete oxidation has been added. To the left of this point of intersection, the separation of the two steps is greater.

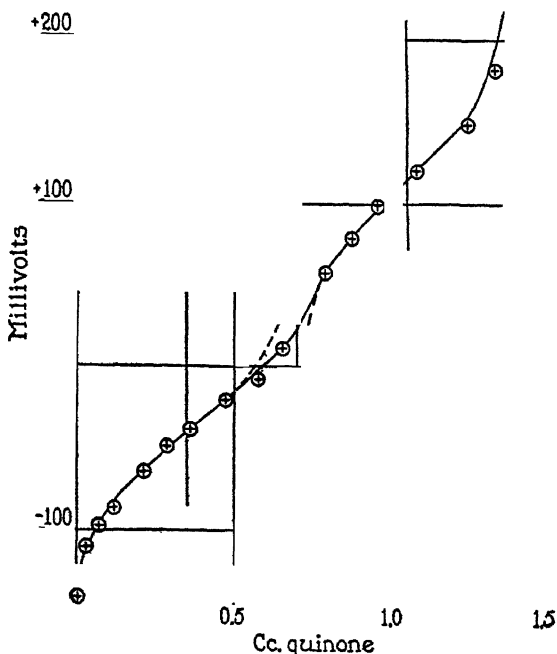


FIG. 7. Reduced α -oxyphenazine at pH 1.86 is titrated with quinone. Potentials referred to the normal hydrogen electrode.

Secondly, notice at pH 1.3 a bend in the E_m and in the E_1 curves, but none in the E_2 curve. To interpret these bends we apply the rules of W. M. Clark and B. Cohen (3), which may be expressed as follows: (1) Each bend is correlated with an acidic dissociation constant.⁷ (2) When the curve becomes steeper this constant belongs to the oxidized form of that particular oxidation-reduction system; if flatter, to the reduced form. (3) Each dissociation constant alters the slope by 0.06 volt per pH unit, when

⁷ Applying Brönsted's definition, basic dissociation constants may be included among the acidic ones.

the system is a one-electron system; by 0.03 volt per pH unit, when it is a two-electron system. (4) In order to evaluate graphically the dissociation constant, extend the rectilinear parts of the curves to tangents, which then will intersect. Project the point of intersection on the abscissa. This gives pK.

On applying these rules to the E_1 curve we find at pH 1.3 a change of the slope from 0.06 volt per pH unit to 0.12, the change thus amounting to an increase in slope of 0.06 volt per pH unit. This signifies a $pK = 1.3$ for the oxidized form of a one-electron system. The system is here the T-S system, which really is a one-electron system, and the constant belongs to

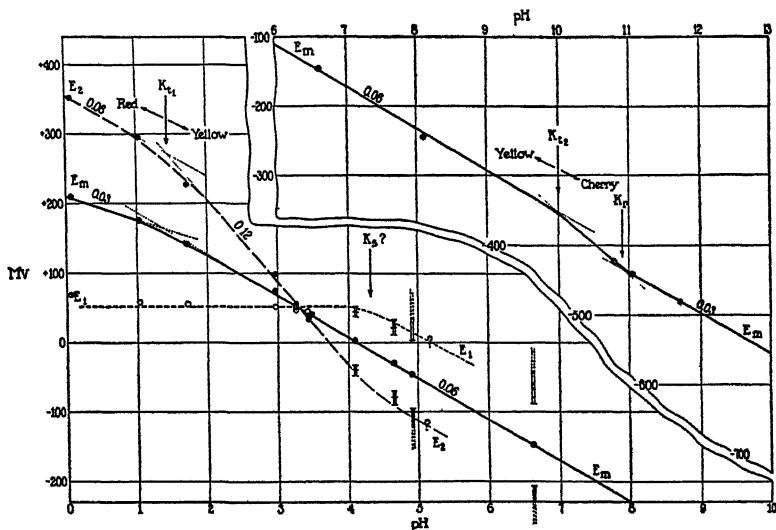


FIG. 8. The three normal potentials E_m , E_1 , and E_2 of α -oxyphenazine plotted against pH (at 30°C.). The ordinate is the potential, in millivolts; the reference potential is a calomel electrode, which is +0.242 volt with respect to the normal hydrogen electrode. The upper curve is an extension of the lower one.

the oxidized form of this system. At the same pH we notice in the E_m curve a change of slope amounting only to 0.03 volt per pH unit, indicating a dissociation constant of a two-electron system. This is the T-R system, and this bend is a confirmation of the result obtained from the E_2 curve. The E_1 curve shows no bend at this pH. This curve belongs to the S-R system. The T form, whose constant becomes manifest at this pH in the two other curves, cannot have and does not have any influence on the slope of the E_1 curve. The existence of a $pK = 1.3$ is corroborated by the fact that around pH 1.3 the color of the oxidized form turns from yellow to red.

On pursuing the three normal potential curves to the right of the cross-

ing, the limits of error in drawing the E_1 and E_2 curves become greater as these curves begin to diverge. For, from table 1 one can infer that, as the index potential approaches its minimum value of 0.0143 volt, an error of a few tenths of a millivolt in the index potential involves a conspicuous error in E_1 and E_2 . Only E_m is unaffected with respect to the limits of error throughout all pH ranges. In figure 8 the influence of such a limit of error in E_1 and E_2 is symbolized, assuming the limit of error in E_1 to be ± 0.5 millivolt. Thus, it is of no use to extend the E_1 and E_2 curve too far beyond the point of intersection. It seems that at pH 4.2 these curves may have

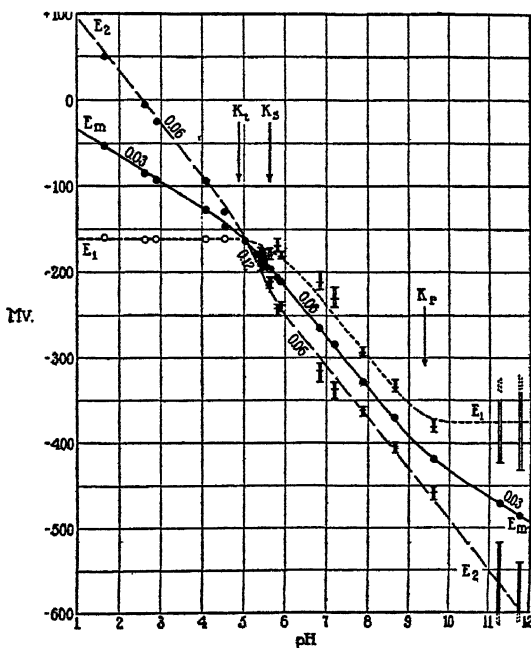


FIG. 9. The three normal potentials of pyocyanine plotted against pH. Designations as in figure 8.

a bend so as to make them, over a certain range, both parallel to the E_m curve. This would signify a dissociation constant of the semiquinone, $pK = 4.2$, if these bends be real.

A second example is that of pyocyanine (α -oxy-*N*-methylphenazine). The curves in figure 9 were established by the above method. Although here also the limits of error at the right-hand side of the point of intersection are appreciable, they are not quite so disturbing as in the foregoing case, and there is some justification in assuming that the bends in E_1 and E_2 at pH 5.6 are real, and that these curves both become parallel to the E_m

curve up to pH about 9. This agrees very well with the observation that, on oxidizing the colorless reduced form at pH 7 to 8, the color first turns greenish blue and on further oxidation a pure blue, whereas at pH 11 the color turns directly blue and thereafter only becomes more intensely so. In the interval of parallelism, $E_2 - E_1 = 0.070$ volt, approximately. This, according to table 1, would mean $K = 0.05$ approximately, and would allow, according to figure 4, for about 10 per cent of the dye to exist in the semiquinoid form in the midpoint of titration even in slightly alkaline solutions, a fact that may have a physiological bearing.

THE CONDITION FOR THE EXISTENCE OF SEMIQUINONES

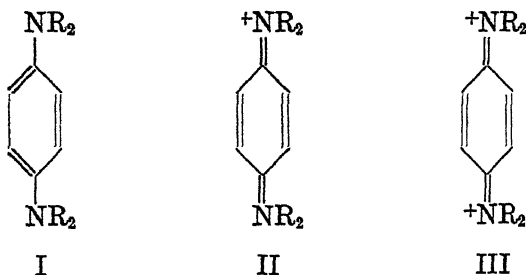
The occurrence of a semiquinone on partial reduction of a quinoid substance or on partial oxidation of a benzenoid substance may be interfered with for two very different reasons. In the first place the formation constant K may be extremely small or zero. Consequently, as K in general depends on pH, the semiquinone may exist at certain pH values, but not at others, as has been shown in the two examples just now presented. If K is very small but the semiquinone very little soluble, the semiquinone may exist only in the solid state, as is the case for quinhydrone. Also the semiquinoid form of chlororaphine is so difficultly soluble that in cultures of *Bacillus chlororaphis* it crystallizes within the liquid medium without the culture medium itself showing the green color of the semiquinone, as will be discussed in detail later on.

In the second place, the semiquinoid, being an unsaturated radical, may be liable to a more or less rapid irreversible rearrangement into substances different from the parent substances. The two conditions of existence may be distinguished as the thermodynamic condition and the stability condition. The first one may be stated thus: the dismutation constant must not be too large. The other may be stated as follows: the semiquinone must not be too fragile a molecule. All transitions may occur. So, as will be discussed in the special chemical part of this review, the lability of the semiquinones of *p*-phenylenediamine derivatives varies considerably according to substitutions in the amino groups. But among the three constituents of a two-step system it is not always the semiquinoid that exhibits the greatest instability. Sometimes it is the quinoid form, e.g., in the aromatic diamines. For this reason, Wurster's blue is perfectly stable in solution only in the presence of an excess of tetramethyl-*p*-phenylenediamine, which establishes the thermodynamic condition by preventing the dismutation of the semiquinone according to equation 4a. In the case of the γ,γ' -dipyridyl compounds, conversely, the oxidized form is perfectly stable, the semiquinoid forms relatively stable; the completely reduced one is labile.

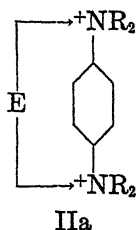
THE BEHAVIOR OF SEMIQUINOID RADICALS AS COMPARED WITH THAT OF
OTHER ORGANIC RADICALS AND ITS INTERPRETATION

Two groups of organic radicals present themselves for comparison with the semiquinoids, those with tervalent carbon as represented by Gomberg's triphenylmethyl, and especially those with bivalent nitrogen as represented by Wieland's diphenylnitride. There are two essential differences. First of all, the compounds of these two groups have no existence in any aqueous solvent, whereas many semiquinones are perfectly stable in water under proper conditions of pH and oxidation-reduction potential. Secondly, the other types have a great tendency to abolish their unsaturated state either by dimerization or by eagerly combining with other reactive molecules, or certain specific substances. The triarylphenyl compounds combine with oxygen to a peroxide $(\text{Ar})_3\text{CO}:\text{OC}(\text{Ar})_3$; the diaryl nitrides add nitric oxide in this way, $(\text{Ar})_2\text{N} + \text{NO} \rightarrow (\text{Ar})_2\text{NNO}$. In the semiquinones, neither a dimerization nor any specific addition reaction has been found as yet. Several of the semiquinones are so perfectly stable even in aqueous solutions in certain pH ranges (of course, except for their sensitivity toward oxidants or reductants), that this contrast to the other types of radicals needs some explanation. The following suggestion is thought to be on the right track.

Taking tetramethyl-*p*-phenylenediamine as an example, we can formulate the three steps as follows:

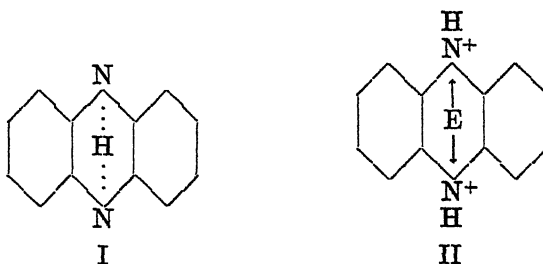


In formula II the lower nitrogen atom is of the character of a free ammonium radical. We now may imagine that the positive charge in II is not permanently at the upper nitrogen atom but oscillates between both nitrogen atoms, as symbolized in IIa, where the electron E is shown to oscillate between two positively charged nitrogen atoms so as to neutralize in rapid succession, now one, now the other charge. This may be considered a structure which might exhibit stability on the ground of the perfect symmetry.



Each positively charged nitrogen means a nitrogen kernel with seven, instead of the usual eight, electrons in the outer shell, and the septets take turns in utilizing the odd electron to fill up the octet. Furthermore, as this molecule is a cation, in contrast to the electroneutral triphenylmethyl or diphenylnitride, electrostatic repulsion will prevent the formation of a double molecule. If we wish to speak of definite paths of the electrons we may say that the odd electron has a path encircling the two nitrogen atoms. As such a wide circuit for an electron appears unlikely, one may rather imagine that the electric oscillation takes place through the whole chain of atoms from one nitrogen to the other. Avoiding any mechanical model, one might simply say that the probability of the odd electron belonging to the one or to the other nitrogen is the same. We may also say that the odd electron is a chemical bond of the two nitrogen atoms, which is presented by a single electron instead of the customary pair of electrons. So the ordinary valence symbols are not suitable to formulate these compounds. The oscillating odd electron may be imagined to be an electric oscillator of especially low frequency and to account for the optical properties to be discussed later on.

In the phenazine group the shared electron may be imagined in two different ways, according to formulas I and II in which E is the electron:



In formula I one hydrogen atom stands between the two nitrogen atoms. The electron of the hydrogen atom completes alternately the septet, now of the one, now of the other nitrogen atom, to an octet. In this case we may also speak of a shared hydrogen atom. In the other form there is one

electron shared by both nitrogen atoms. This formula differs from the other by a proton. The two forms may therefore be considered as two steps of acidic dissociation of the same substance. In fact, there is some evidence that the semiquinone in the phenazine group may exist in two states of acidic dissociation. For, as stated above, there seems to be a dissociation constant of the semiquinone of pyocyanine, $pK = 5.2$.

The occurrence of a dissociation constant in the semiquinoid form may have important consequences. In the case of pyocyanine, it brings about the parallelism of the three normal potentials over a certain pH range. Hence, the thermodynamic condition for the existence of the semiquinone remains constant within this pH range. According to circumstances, such a dissociation constant may have all kinds of peculiar consequences. One of them may be mentioned because later on a case will be shown where it seems to occur. Let us assume that the E_m curve has a 0.03 slope around the common point of intersection, and that the E_1 curve lies above the E_m

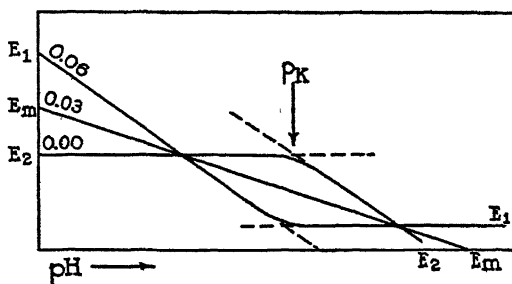
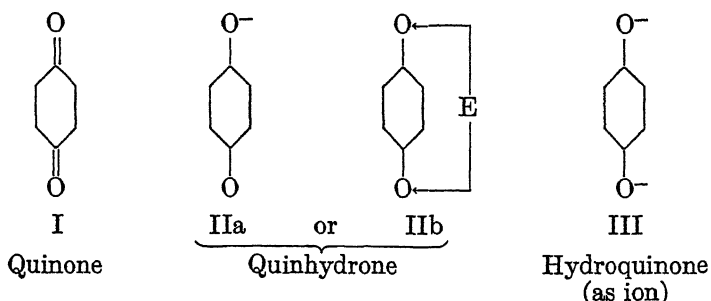


FIG. 10

curve to the left from this point of intersection (figure 10). When now the semiquinoid happens to have a dissociation constant, so that $pK >$ the pH at the point of intersection, the bend brought about will cause once more an intersection. In such a case the thermodynamic condition for the existence of the semiquinone is restricted to a limited pH range and is at a maximum when $pH = pK$.

ANIONIC SEMIQUINONES

The above interpretation of the structure of a semiquinone holds for the case of its being a cation. The question will now be raised whether there are also anionic semiquinones. The simplest example imaginable would be that of quinhydrone (formulas I to III). This case is not accessible to a potentiometric investigation. The dark green crystals of quinhydrone when dissolved at $pH < 7$ do not show any color resembling that of the



crystals. When hydroquinone at $\text{pH} < 7$ is titrated with an oxidant, the titration curve is precisely the one of an ordinary two-electron oxidation without step formation. So no form intermediate between quinone and hydroquinone exists in an acid solution. This fact may also be stated in the following form. Quinhydrone dissolved in an acid solution dismutates completely into quinone and hydroquinone, the dismutation constant being extremely large. Since for cationic semiquinones the dismutation constant decreases with *decreasing* pH, one might infer that for anionic semiquinones this constant would decrease with *increasing* pH instead. In other words, the thermodynamic condition for the existence of an anionic radical would increase with increasing pH. In fact, alkaline solutions of quinhydrone exhibit a strong color, but unfortunately the stability condition is impaired by alkali. Secondary irreversible rearrangements take place. The color developed is not only that of the semiquinone, but is probably due even more to secondary reactions, and no constant potentials can be obtained in alkaline solutions. Concerning the solid crystalline quinhydrone, Foz and Palacios conclude from an x-ray analysis that the elementary unit of the quinhydrone crystal is the monomolecular radical, not any bimolecular unit.

It seems likely that the indigo dyes belong to this group and offer a better chance for a potentiometric investigation. What is known at the present time along these lines will be shown in the special chemical section of this review.

PRELIMINARY REVIEW ON THE OPTICAL PROPERTIES OF THE SEMIQUINONES

The odd electron supposedly present in all semiquinones and oscillating between two atoms intramolecularly renders these substances a desirable subject for spectroscopic studies. Although these are not far enough advanced for any theoretical treatment, yet the essential features may be mentioned. It seems that all semiquinones exhibit a remarkably distinct band spectrum. This is simplest in the viologen dyes. Here we have in the visible region a single distinct band which very likely will be suitable

for a study of a finer structure. The maximum absorption lies in the red or yellow, drops rather steeply toward the longer wave lengths and more gradually toward the shorter wave lengths, forming here a secondary, less distinct maximum. In the hand spectroscope one has the impression of a strong band followed by a weaker one. Only in benzylviologen is the first band weaker than the second. This dye undergoes a very remarkable and reversible change of light absorption with temperature, a fact that was already known to Weitz and Piccard. The color appears violet at room temperature and blue at about 80°C. Spectroscopically, the change is not so much attended by a shift of the absorption maxima to different wave lengths but rather by a change in intensity of the two absorption maxima; the higher peak becomes the smaller one and vice versa. To a very small extent a similar phenomenon can be observed in the other viologens, but not in the violet dye produced from γ,γ' -dipyridyl itself.

Wurster's dyes, the oxidation products of the substituted phenylene diamines, show the same type of band, but this band is, in all its details, repeated in an interval of about 300 Ångström units, and this second band overlaps with the first. The semiquinones of the phenazine series, mostly green in color, have no definite band in the visible, but in the one example investigated by Hantzsch there is a double band in the ultra-violet. The semiquinoids of the indigo dyes show a very sharp single band in the visible spectrum.

It may also be expected that semiquinones may show paramagnetic properties, according to Taylor and Lewis (51). Kenyon and Sugden (27) also found paramagnetism in a colored compound of supposedly radical character, which however cannot be properly counted to the semiquinones. For these compounds the study of magnetic properties has still to be carried out.

SPECIAL CHEMICAL PART

1. *p*-Phenylenediamine group

The first product on oxidizing *p*-phenylenediamine in a moderately acid solution is too labile and not suitable for a detailed investigation. On oxidizing, e.g. with bromine, a very transient yellow arises, turning to green, red, and finally becoming colorless.

Substitution of the amino hydrogens of *p*-phenylenediamine leads to compounds having two distinctly different steps of oxidation. Table 2 has been established by Piccard (44). Of these compounds the asymmetrical dimethyl and diethyl, the tetramethyl and tetraethyl, and the symmetrical diphenyl derivatives have been subjected by the writer to a potentiometric study (42). The diphenyl compound is easiest to under-

TABLE 2
Oxidation steps of derivatives of p-phenylenediamine

LEUCO BASE	HOLOQUINOID SALT	MERQUINOID SALT
$\text{H}_2\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{NH}_2$	Colorless	Yellow
$\text{H}_2\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{NH}(\text{CH}_3)$	Colorless	Red-yellow
$\text{H}_2\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{N}(\text{CH}_3)_2$	Colorless	Red
$\text{H}_2\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{NH}(\text{C}_6\text{H}_5)$	Yellow	Red
$\text{H}(\text{CH}_3)\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{N}(\text{CH}_3)_2$	Colorless	Violet
$(\text{CH}_3)_2\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{N}(\text{CH}_3)_2$	Yellowish	Blue
$(\text{CH}_3)_2\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{NH}(\text{C}_6\text{H}_5)$	Yellow	Blue
$\text{H}(\text{C}_6\text{H}_5)\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{N}(\text{C}_6\text{H}_5)\text{H}$	Red	Blue (greenish)
$(\text{C}_6\text{H}_5)_2\text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{N}(\text{C}_6\text{H}_5)_2$	Blue	Green

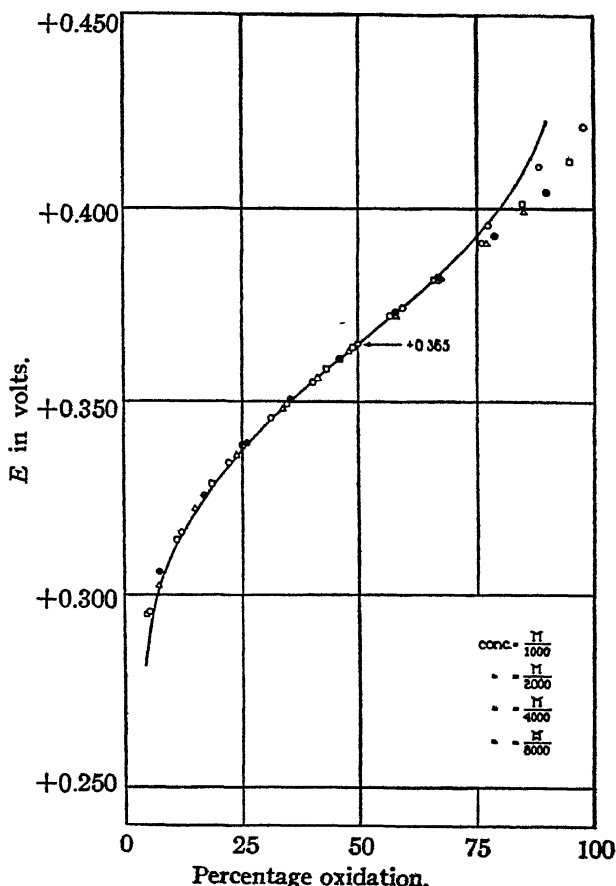


FIG. 11. Independence of the normal potentials of tetramethyl- p -phenylenediamine on the initial concentration. Potentials are plotted against percentage of oxidation; ordinate is potential in volts; abscissa is percentage of oxidation. Potentials referred to the normal hydrogen electrode. pH 4.620, varying no more than ± 0.01 in the individual titration experiments.

stand, both steps of oxidation being stable compounds so that definitive and non-drifting potentials could be obtained using 90 per cent acetic acid + 10 per cent water as a solvent and bromine as oxidant. The two steps of oxidation are easily distinguished, being separated by a definite jump. The separation happens to be so great that very little overlapping of the two steps takes place, and each half of the curve shows the shape of an ordinary one-electron curve. The substance is unfortunately not sufficiently water-soluble to allow establishment of a set of titration curves in aqueous buffer solutions. This can be carried out with the tetramethyl

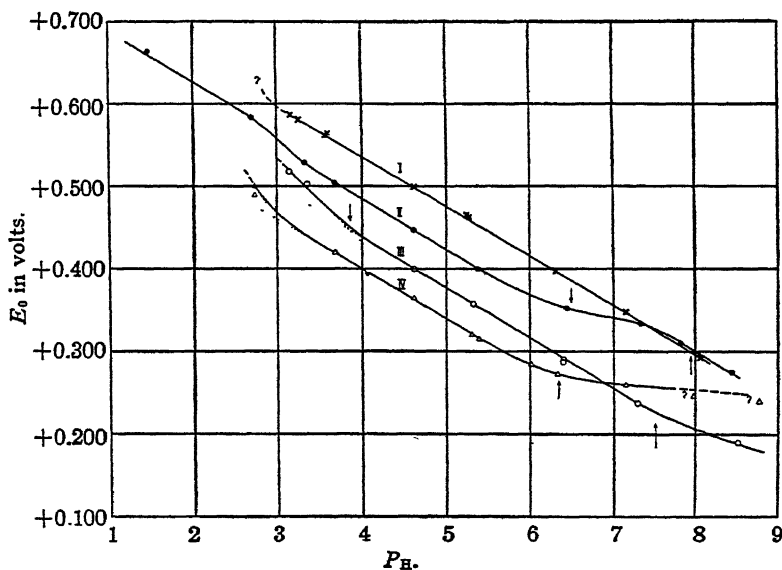
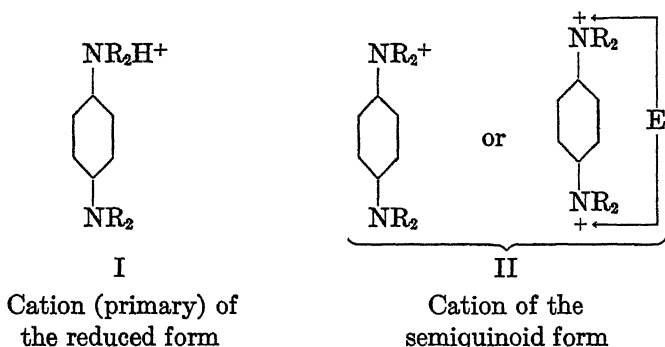


FIG. 12. Normal potentials are plotted against pH for the four alkylated diamines as follows: X, diethyl-*p*-phenylenediamine; ●, dimethyl-*p*-phenylenediamine; O, tetraethyl-*p*-phenylenediamine; Δ, tetramethyl-*p*-phenylenediamine. Ordinates, normal potentials in volts; abscissas, pH. Potentials referred to the normal hydrogen electrode.

or tetraethyl compound. Here, however, the holoquinoid form, a bi-quaternary iminium base, is an extremely labile compound, so the titration can be carried out only for the first step of oxidation and not even here to completeness. The two steps are not distinctly enough separated as to prevent some overlapping. Therefore the potentials are definite only up to about 60 to 65 per cent of the oxidation to the first step. On the other hand, this substance is very suitable for showing that the shape of the titration curve does not depend on the initial concentration of the substance, as shown in figure 11. In this figure the rudimentary titration curve, as

obtained from the non-drifting part of the oxidation, has been extrapolated to a full theoretical curve. In the range of oxidation greater than 70 per cent it no longer fits the experimental data, in part because of the uncertainty of the measurements owing to the drift, in part because of the overlapping of the two steps which, although seemingly not very great, necessarily causes a deformation of the curve. Such titration curves can be obtained throughout a pH range of about 3 to 7. The normal potentials plotted against pH as shown in figure 12 lie on a straight line with a slope of 0.06 volt per pH unit. This indicates that the oxidized and the reduced form differ not only by an electron but by a full hydrogen atom. This is in agreement with the formulas 1 and 2 expressing the state of ionization of



these compounds in a moderately acid solution. At pH approximately 6.5, the slope of the curve apparently is changed in such a way as to indicate a dissociation constant of the reduced form, the magnitude of which agrees with the dissociation constant directly determined. This part of the curve, however, cannot be pursued to higher pH values, as then the potentials show a drift even in the first part of the titration. Something similar takes place on the left-hand end of the curves of figure 12, owing to another dissociation constant.

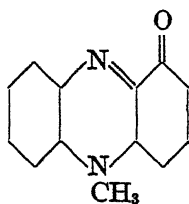
In the same figure there are also shown the results for the tetraethyl, the dimethyl, and the diethyl compounds. The dialkyl compounds can be titrated almost as well, but the potentials are not quite so stable as in the tetraalkyl compounds, even in the first part of the titration. This behavior is a transition to that of the unmethylated compound, which is not suitable for a titration at all, as stated above.

2. The phenazine group

(a) *Phenazine*. Phenazine itself is not water-soluble enough for a complete study in aqueous buffer solutions. It gives most satisfactory results in 50 per cent acetic acid solution, titrated with quinone, dissolved in the

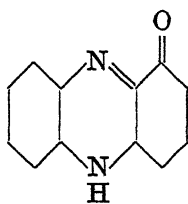
same solvent. The curve shows two distinctly separated steps which agree perfectly in shape with two one-electron titration curves, the normal potentials amounting to -0.086 and $+0.254$ volt, in this solvent, which has an (apparent) pH of 1.26.

Several derivatives of phenazine are water-soluble enough to allow a complete set of experiments in aqueous buffer solutions over a wide range of pH.

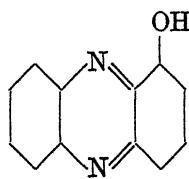


I

Pyocyanine

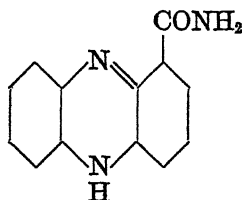


IIa



IIb

Two tautomeric formulas for
 α -oxyphenazine

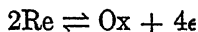


III

Xanthoraphine
(or "oxychlororaphine")

(b) *Pyocyanine*. Pyocyanine, the blue pigment of *Bacillus pyocyaneus*, a saprophyte frequently encountered in purulent wounds, has been synthesized by Wrede and Strack (64, 65). They established the formula shown above except for the fact that they ascribed to it the double-molecular size, assuming that two molecules are bound together in such a way that the non-methylated nitrogen atoms are pentavalent and linked together by a double bond. For the completely reduced form they assume the monomolecular formula. The intermediate form escaped their attention, although they mention that on reducing the dye, a transient green color arises. The bimolecular formula of pyocyanine was based on a determination of the freezing point of the free base in glacial acetic acid. Without deprecating these authors' merit in the analysis and synthesis of this substance, their conclusion as to the molecular weight cannot be accepted.

We may consider this as another case of misleading results of a freezing point determination. It cannot be definitely excluded that in glacial acetic acid in such a high concentration of the dye as needed for the experiment a partial association may take place. It is equally possible that the large amount of dye dissolved in the solvent exceeds the solubility at freezing point temperature. In any case the bimolecular formula is untenable for a dilute aqueous solution. For in this case the equation of the reduction in a solution sufficiently alkaline to prevent the formation of the semiquinone would read



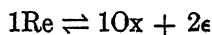
where Ox is the oxidized form and Re the reduced, which Wrede also assumes to be monomolecular. In this case the equation for the potential should be

$$E = \text{Const.} + \frac{RT}{4F} \ln \frac{[\text{Ox}]}{[\text{Re}]^2}$$

Whereas in reality the titration curve follows quite strictly the equation

$$E = \text{Const.} + \frac{RT}{2F} \ln \frac{[\text{Ox}]}{[\text{Re}]}$$

This necessarily leads to the chemical equation



and is in agreement only with the monomolecular form and entirely analogous to the other known phenazine compounds.

It has already been stated above that within the physiological pH range from 6–8 an appreciable amount of the semiquinone is capable of existence at a suitable oxidation–reduction potential in spite of the considerable overlapping of the two halves of the titration curves. The result of the potentiometric study of pyocyanine has already been shown in figure 9.

(c) *Chlororaphine*. *Bacillus chlororaphis* Guignard and Sauvagneau produces in its cultures a yellow pigment, xanthoraphine or oxychlororaphine, prepared by P. H. Lasseur (35). In the culture medium there is developed under certain circumstances a crystalline green pigment called chlororaphine. Kögl and Postowsky (28) succeeded in elucidating the constitution of these dyes. Oxychlororaphine was found to be phenazine- α -carbonamide. It could be reduced to chlororaphine and in a second step to a dihydro compound, yellow in color. When this dihydro compound and oxychlororaphine are dissolved in glacial acetic acid no color change occurs, but on addition of water green crystals of chlororaphine are precipitated.

The authors therefore ascribed to chlororaphine the constitution of a meriquinone in Willstätter's sense. In a later paper (30) under the influence of the results obtained on pyocyanine, as just discussed, they changed their point of view and accepted the monomolecular radical formula for chlororaphine. They determined the freezing point of a mixture of the fully oxidized and the fully reduced form in camphor and found in solutions from 3-7 per cent a molecular weight from 219 to 372, increasing with concentration, the theoretical value of the dimolecular compound being 448. Although here with increasing concentration quite obviously some kind of association takes place, no green color is developed in camphor solution. This shows that the intermediate compound does not exist in camphor, the dismutation constant being too high, and that the association at higher concentration has nothing to do with the green compound. The freezing point data, therefore, cannot be utilized to decide upon the molecular size of the green chlororaphine. They are rather due to the general occurrence of partial association of dissolved molecules, especially in organic solvents, at high concentrations. Once more it is shown how precarious is the interpretation of freezing point data. Their hypothesis of chlororaphine being a monomolecular semiquinone was entirely confirmed by Elema's (10) potentiometric studies. He showed that in a very acid aqueous solution at a sufficiently low concentration all three steps of oxidation-reduction are sufficiently soluble to allow a potentiometric titration in an homogeneous system. On reduction the color turns from light yellow to an intense emerald green and then to orange yellow, the latter being the color of the dihydro compound. Utilizing the theory of the two-step oxidation, in the way illustrated above, he arrived at the result shown in figure 13. This figure shows the crossing-point of the three normal potentials at pH 2.1, indicating that at this pH the formation constant = 1. The extension of the E_1 and E_2 curve towards the right-hand side of the crossing-point can only be approximately estimated for the reasons discussed above. Yet it seems that the E_1 and E_2 curves, which might have been expected to diverge to the right-hand side of the crossing-point, very soon begin to converge once more, so as to become parallel to each other and to the E_m curve. If this be so, it would indicate that the formation constant of the semiquinone at the right side from the crossing, although it may be small, remains constant over a certain pH range and so is compatible with the formation of the radical even at higher pH. The semiquinone being extremely difficultly soluble at this pH, the formation of its crystallized form in the cultures is explained.

(d) *Other phenazine compounds.* The case of α -oxyphenazine, a dye first synthesized by Wrede and Strack as an intermediate product during the synthesis of pyocyanine, has been already presented as an example for

an especially illustrative instance of a two-step system (figure 8). In a great number of other phenazine compounds intermediate states of oxidation-reduction can be observed, although they have not been subjected to potentiometric study. Not only in the class of the phenazines proper, but also in the group of quaternary phenazonium compounds (safranines), it is remarkable that a semiquinone has never been observed in a compound containing one or more free amino groups as side chains to the benzene

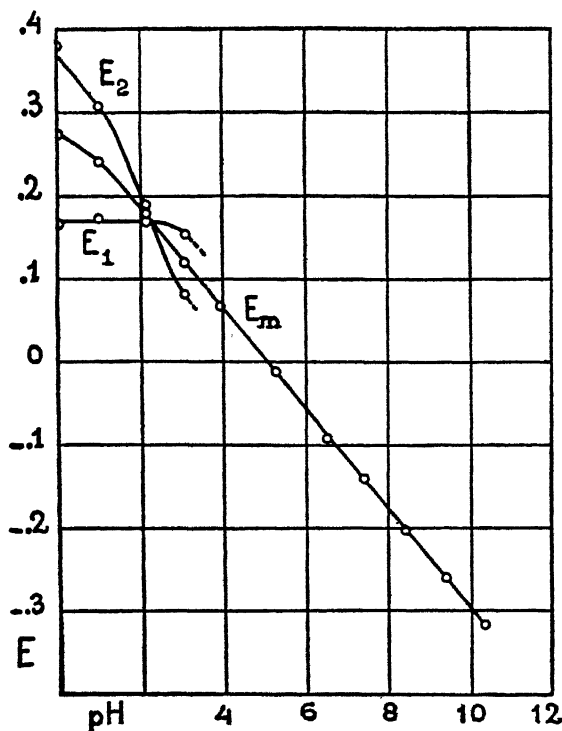
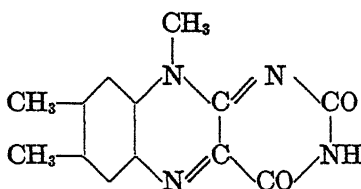


FIG. 13. The three normal potentials of the chlororaphine system plotted against pH, according to Elema.

rings (42). The following compounds showed no intermediate form of reduction: symmetrical and asymmetrical diaminophenazine, triaminophenazine, *m*-methylrosinduline, *N*-dimethylisorosinduline, asymmetrical anilinoaminophenazine, aminoacridine, asymmetrical aminohydroxyphenazine, rosinduline, isorosinduline, phenylacridine. Semiquinones have been observed in phenazine, α -oxyphenazine, α -methoxyphenazine, α -oxy-*N*-methylphenazine (pyocyanine), α -carbonamidephenazine (chlororaphine), phenyl-naphthazonium nitrate, phenylisonaphthazonium nitrate,

methylnaphthazonium chloride, rosindonesulfonate, (rosinduline GG). In all phenazine and phenazonium compounds the semiquinoid is green, and in all naphthophenazine compounds, including rosindonesulfonate, it is red to violet. The oldest known green intermediate form is that of phenazine itself, observed as early as 1873 by Claus. The corresponding form for methylphenazonium compounds was the subject of a heated discussion between Kehrmann and Hantzsch, during which Hantzsch first advocated the radical formula.

(e) *The flavin group.* Warburg and Christian (54) prepared a yellow compound, the "yellow respiration enzyme," from yeast, recently also in the crystallized state. This substance can be easily split into a colorless part, probably a protein, and a yellow pigment. This has now been recognized to be a dyestuff, called photoflavin, combined with a side chain consisting of a pentosephosphate ester (31, 32, 33; 52). Warburg discovered that this side chain is detached on illumination with visible light in alkaline solution. From this, free "photoflavin" can be extracted by chloroform. In the meantime R. Kuhn and his associates, Ellinger and Koschara (14), and K. G. Stern (48, 49) found representatives of this class of dyestuffs widely distributed in animal and vegetable tissues and fluids. The photoflavins derived from the representatives of this group seem to be alike or at least very closely related. R. Kuhn ascribes to lactophotoflavin, prepared from milk, the constitution of a substituted isoalloxazine (see formula). The resemblance of its structure

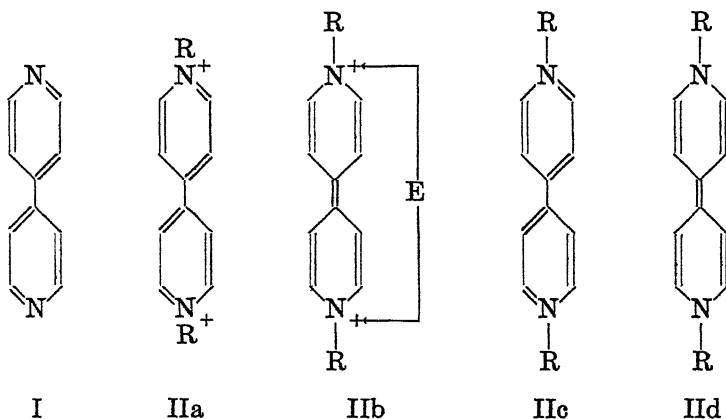


to pyocyanine is obvious. Homologous substances of similar properties have been synthesized by R. Kuhn and his associates, and by K. G. Stern and Holiday. These dyestuffs can be reversibly reduced to leuco compounds. Kuhn and Wagner-Jauregg discovered (32) that this reversible reduction, when performed in a strongly acid solution, passes through an intermediate stage of red color. They advanced the hypothesis that this is due to formation of a semiquinone. This problem has been studied potentiometrically by K. G. Stern (48) with photohepatoflavin and with photoyeastflavin, and by Barron and Hastings (1) with lactoflavin. The latter authors obtained distinct two-step curves in acid pH ranges, but they have not yet published the details. Stern found that in neutral and alkaline solutions the titration curve of the dye resembles

very closely the one of an ordinary reversible organic dyestuff with the electron number 2. In the acid range, the slopes of the curves become increasingly steeper with decrease of pH, and in very acid solution, pH 0.4 to 0.2, a distinct step in the titration curve takes place, indicating all characteristics of semiquinone formation. On plotting the three normal potential curves against pH, a graph similar to that of pyocyanine is obtained, the common point of intersection lying at pH 2.2. To the right of this point, the E_1 and E_2 curves seem to converge so as to become approximately parallel to the E_m curve, as it is with pyocyanine. The data available in the range from pH 2.2 to 14 do not seem precisely enough known to allow accurate drawing of the E_1 and E_2 curves throughout this range. In this range, a slight error in the determination of the index potential involves a great error in E_1 and E_2 , as has been shown above. The scarcity of the material then available was not favorable to obtaining quite precise determinations in this region. But the data available at least seemed to indicate that the thermodynamical existence condition of a semiquinone remains approximately constant throughout this range. So it is likely that the semiquinone is capable of existence even in neutral and alkaline solution, if only to a slight extent. Visible semiquinone formation is limited to the range of pH < 2. It should be mentioned that Bierich and Lang (2), working with a similar, or perhaps even identical pigment extracted from various organs, had obtained titration curves which showed no indication of any step formation.

(f) *The benzidine group.* Benzidine and tolidine can be oxidized in an acid solution to intensely green or blue compounds and, furthermore, to a second step of oxidation of brown color. The same holds for their derivatives such as those in which the hydrogen atoms of the benzene rings are substituted by halogens or those of the amino groups are substituted by alkyls. Schlenk (46) proved the blue or green compounds to be of the oxidation level of a meriquinone, and accordingly formulated them as bimolecular compounds. In general they are of very unstable nature, even in dry condition. A potentiometric study was attempted by Sullivan, Cohen, and W. M. Clark (50). The unstable nature and the ensuing drift of the potentials was unfavorable to an interpretation of the reactions involved. In very acid solution no intermediate green compound is formed; the oxidation leads directly to the second step, and in this case the authors obtained an ordinary two-electron curve. The writer attempted titration experiments with many benzidine derivatives without encountering any one in which the intermediate step of oxidation was sufficiently stable to obtain an interpretable titration curve. For this reason the molecular size of these products cannot yet be decided. There is no proof as yet that these compounds are of the same nature as those of the other groups described.

(g) *The dipyridyl group.* When γ,γ' -dipyridyl dissolved in diluted acetic acid is reduced by chromous chloride, a deep violet color is developed. On reduction with zinc dust the reduction passes through the same violet stage to a second colorless one. The violet dyestuff has been shown by Dimroth and Heene (8) to be on the oxidation level of a quinhydrone, intermediate between dipyridyl and dihydrodipyridyl. The violet color does not appear when the reduction is performed in a neutral or alkaline medium. Dipyridyl can easily be converted into a biquaternary base, each nitrogen adding, e.g., one methyl-halogen. These quaternary



I. γ,γ' -Dipyridyl.

IIa. Cation of a biquaternary compound of I (viologen).

IIb. The semiquinoid form obtained by partial reduction of IIa (E is an electron).

IIc and IId. Two tautomeric formulas of the second step of reduction; IIc is a double ammonium radical, the nitrogen atom being apparently "quadrivalent."

bases, especially dibenzyl- γ,γ' -dipyridylium diiodide, were already known to W. H. Hofmann, although he did not realize their true constitution. We shall refer to these quaternary bases as viologens, e.g., dimethyl- γ,γ' -dipyridylium dichloride will be designated methylviologen (43). All viologens can be reduced in a first step to violet dyes. Besides, substances of a further reduction level, namely, on the level of dihydrodipyridyl, are known. They have been prepared by E. Weitz, are light brown in color and very little soluble in water. He showed that they may be considered with the same justification as derivatives of dihydrodipyridyl or as free ammonium radicals as in formula IIc. The reduction of the quaternary bases of γ,γ' -dipyridyl leads to violet dyestuffs, not only in an acid solution

as is the case for free γ, γ' -dipyridyl, but also in alkaline solution. In this case sodium hydrosulfite can be used as reductant. The violet dye prepared by partial reduction of benzylviologen was isolated in crystalline form by E. Weitz. This is that particular semiquinoid compound in which he succeeded in establishing the molecular weight as mentioned above, by the boiling point method. He found it to be compatible only with the semiquinoid radical formula. It will be clear now even more so than above that this determination was favored by unusual circumstances. In order to obtain correct results by this method, the condition must be fulfilled that the semiquinone, dissolved in the solvent, undergoes no dismutation according to equation 4a. Such a possibility was not even considered by Weitz. However, the potentiometric method confirmed this result.

The titration experiment obtained by reducing the viologens (42) with sodium hydrosulfite showed potentials of a fairly stable nature (see table 3).

TABLE 3
Normal potential of viologens
(Independent of pH) at 30°C., referred to the normal hydrogen electrode

VIOLOGENS	NORMAL POTENTIALS
	<i>volts</i>
Methylviologen.....	-0.446
Ethylviologen.....	-0.449
Betaineviologen.....	-0.444
Benzylviologen.....	-0.359

The very slight drift of these potentials amounting to 0.1 to 2.0 millivolts per minute did not cause any serious trouble in the characterization of the titration curve obtained and left no doubt that the violet dye is a semiquinone of the same molecular size as the colorless viologen itself. The normal potentials are listed in table 3 and were independent of pH within the range accessible to experimentation, pH about 8 to 12. This range is limited, owing to the very negative level of the potential. For methylviologen, e.g., the normal potential approximately equals the potential of the hydrogen electrode (one atmosphere pressure of hydrogen) at the same pH. This normal potential, being independent of pH, therefore is in the hydrogen overvoltage range at $\text{pH} < 7$, and for this reason not suitable for a titration experiment in an acid solution. But even in distinctly acid solution viologen will be reduced by very strong reductants such as chromous chloride, providing that there is absent a catalyst such as colloidal palladium, which would immediately break down any hydrogen overvolt-

age potential. The viologens can therefore be used as oxidation-reduction indicators, even in a hydrogen overvoltage range, and are unique in this respect. As to the cause of the slight drift of the potential, the writer was inclined to the assumption that it is due to unavoidable minute traces of oxygen, even in the purified nitrogen used during the titration experiment, but now favors rather the assumption that the semiquinoid radical is not a perfectly stable molecule. This idea is suggested by the fact that γ,γ' -dipyridyl itself when titrated in an acid solution by chromous acetate shows very drifting potentials. Furthermore, that viologens containing long carbon chains as side chains always show strong drifts during the titration, and obviously furnish very labile reduction products. This was especially observed (unpublished experiment) in the following case: bromotetraacetylglucose, which, according to Emil Fischer (16), adds to pyridine to form a quaternary base, can also be attached to γ,γ' -dipyridyl. This compound can easily be freed from its acetyl groups. So, a glucose-viologen (or rather a glucosylviologen) is obtained which on reduction in alkaline solution also produces a blue dye. This, however, is much more labile than the others. Another very labile semiquinone is the one obtained by reduction of hydroxyethylviologen, prepared from γ,γ' -dipyridyl and iodoethyl alcohol. So it may be justifiable to assume that as to the lability of the semiquinone there is only a quantitative gradation according to the nature of the side chain.

The second step of the titration leading from the violet dye to the compounds of the oxidation level of dihydrodipyridyl cannot be followed potentiometrically. In the case of benzylviologen this second step of oxidation is practically insoluble, and so when the first step of titration has been completed, a continuation of the reduction will not change the potential any more. In the case of methylviologens and the others, the second step of reduction lies in too high a hydrogen overvoltage to be manageable.

(h) *The indigo group.* Willstätter some years ago drew the writer's attention to the fact that indigo dissolved in organic solvents, under certain conditions on reduction shows an intermediate red color. Shaffer found that the indigosulfonates when dissolved in a strongly alkaline aqueous solution, on reduction pass through a cherry-red intermediate state. This has been published so far by Preisler and Shaffer only in the mimeographed abstracts of the meeting of the American Chemical Society.* I owe more information about his experimental data to a personal communication and can confirm these authors' main results by my own experiments. When indigodisulfonate is reduced at pH up to about 10, ordinary potential curves are obtained as in most organic dyestuffs, as has been al-

* Meeting held in Chicago, April, 1933.

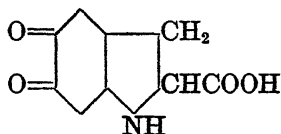
ready published by Sullivan, Cohen, and Clark (50). When the dye is reduced at $\text{pH} > 10.5$, a new phenomenon arises that escaped the attention of the latter authors. An intermediate red color is developed, and at the same time the shape of the titration curve is distorted so as to indicate a two-step reduction. The intermediate form may be either a bimolecular meriquinone, or a semiquinone; in this case there is even a third possibility. Considering the formula of indigo which consists of two perfectly symmetrical halves held together only by a double bond between two carbon atoms, one may be inclined to consider the intermediate form as a radical generated by dissociation of the molecule into two halves by breakage of the bond between the carbon atoms. However, two observations can be pointed out which are compatible only with a semiquinone of the same molecular size as indigo itself. The first, shown by Loeffel in Shaffer's laboratory (36), is this: The semiquinones of the indigo dyes have a distinct absorption spectrum consisting of one single distinct band different for the mono-, the di-, the tri-, and the tetra-sulfonate. Now, if the intermediate form were a molecule of half molecular size, in the case of the trisulfonate the spectrum of the purple radical would be an overlapping of that of disulfonate and the tetrasulfonate radical. This is, however, not the case; the trisulfonate compound has a spectrum of its own. I may add another reason. The shape of the titration curve even at such a pH where the step formation is distinct, is independent of the initial concentration of the dye. This is, as stated above, compatible only with the assumption that the intermediate form has the same molecular size as the oxidized or the reduced one.

As for the details, I do not wish to anticipate Shaffer's publication, but only to state the main features as I could see them from some preliminary experiments of my own. The three normal potentials can be plotted in the same way as shown above for α -oxyphenazine. The common crossing-point of the three normal potentials lies for indigodisulfonate at about $\text{pH} 11$. Around this pH the slope of E_m is a 0.03 one, that of E_1 is a 0.06 one, and that of E_2 is a 0.00 one. Whereas for oxyphenazine E_1 is more negative than E_2 at pH smaller than that of the crossing-point, this is the case for indigo at pH greater than that of the crossing-point. This involves the fact that the thermodynamic condition of existence is improved with increasing pH , in contrast to the case of the phenazines. This is reminiscent of the behavior of quinhydrone, as discussed above, and suggests the idea that the indigo radical is an anionic one. In order to account for such an assumption, one would have to assume that leuco-indigo, like hydroquinone, contains two hydrogen atoms of a weakly acidic character. The hydrogen atoms of the sulfonic groups can play no rôle in this respect, as they are very strongly acidic. It is likely that the two

hydrogen atoms attached to indigo on reduction are slightly acidic, and in this respect complete the analogy with those two hydrogen atoms of hydroquinone which are detached on oxidation.

On increasing the pH beyond 12 the stability of the system is impaired. The drift of potential is, however, not large enough to prevent the establishment of approximate titration curves and estimations of the index potentials. From these it can be seen that the E_1 and E_2 curves first diverge from the E_m curve after the common point of intersection. Thereafter they appear to converge again so as to intersect once more. We cannot yet be quite sure about this assertion. The instability of the system at pH > 12, involving drifts of the potentials, may lead to erroneous conclusions. If the second intersection of the curve be real, it can, in the writer's opinion, be only explained by a dissociation constant of the semiquinone, pK about 12. Here the case seems to be realized, referred to above, that the existence of the semiquinone is restricted to a limited, rather narrow pH range.

(i) *Hallachrome*. A case of semiquinone formation quite unique as yet has been recently described. Mazza and Stolfi (36a) isolated from a marine worm of the gulf of Naples, a polychaete, named *Halla parthenopea*, a dyestuff, hallachrome, to which they ascribe the formula



It can be reversibly reduced to a leuco compound which is slightly yellow. E. A. H. Friedheim (20) subjected this dye to a potentiometric investigation. Oxidative or reductive titrations give stable and well reproducible potentials between pH 0.19 and about 10.0. Throughout this whole pH range any titration curve at constant pH is too steep for a two-electron system and too flat for a one-electron system. The curve has throughout this pH range an index potential of 20 millivolts, varying no more than within the limits of error. At pH > 10 the system begins to become labile, but it can be recognized that the index potential becomes > 20 millivolts. The formation constant K of the semiquinone, can be accordingly calculated to be 0.56, and the difference, $E_2 - E_1 = -18$ millivolts (the limits of error estimated ± 6 millivolt), throughout the pH range 0.1 to 10. The negative sign corresponds to the fact that $K < 1$. The maximum amount of semiquinone capable of existence in equilibrium with the other forms of the dye is as little as about 10 per cent or so. For this reason the pure color of the semiquinone is never to be observed, but only a mixed color.

The oxidized form is red at $\text{pH} < 8.53$, and green at $\text{pH} > 8.53$. Why at this pH the E_m curve shows no bend is not clear and needs further investigation. The slope of the E_m curve (and also E_1 and E_2) is 0.06 volt per pH unit. The change of color on oxidizing the reduced form is yellow-brown-red, or yellow-brown-green, according to the pH . The potential range of this dye is very close to that of pyocyanine.

REFERENCES

- (1) BARRON, E. S. G., AND HASTINGS, A. B.: *J. Biol. Chem.*, Proc. **105**, p. vii (1934).
- (2) BIERICH, R., LANG, A., AND ROSENBOHM, A.: *Naturwissenschaften* **21**, 496 (1933); *Z. physiol. Chem.* **223**, 180 (1934).
- (3) CLARK, W. M., AND COHEN, B.: *U. S. Pub. Health Repts.* **38**, 666 (1923).
- (4) CLARK, W. M., COHEN, B., AND GIBBS, H. D.: *U. S. Pub. Health Repts.*, Suppl. No. 54 (1926).
- (5) CLEMO, GEORGE R., AND McILWAIN, HENRY: *J. Chem. Soc.* **1934**, 1991.
- (6) COHEN, B., AND CLARK, W. M.: *U. S. Pub. Health Repts.* **38**, 933 (1923).
- (7) DIMROTH, O., AND FRISTER, F.: *Ber.* **55**, 3693 (1922).
- (8) DIMROTH, O., AND HEENE, R.: *Ber.* **54**, 2934 (1921).
- (9) ELEMA, B., AND SANDERS, A. C.: *Rec. trav. chim.* **50**, 796, 807 (1931).
- (10) ELEMA, B.: *Rec. trav. chim.* **52**, 569 (1933).
- (11) ELEMA, B.: *Rec. trav. chim.* **54**, 76 (1935).
- (12) ELEMA, B.: *J. Biol. Chem.* **100**, No. 1, 149 (1933).
- (14) ELLINGER, P., AND KOSCHARA, W.: *Ber.* **66**, 1411 (1933).
- (15) EMMERT, BRUNO: *Ber.* **47**, 2598 (1914); **49**, 1060 (1916); **50**, 31 (1917); **53**, 370 (1920); **54**, 204 (1921); **57**, 1792 (1924).
- (16) FISCHER, EMIL: *Ber.* **43**, 1750 (1910).
- (17) FOZ, O., AND PALACIOS, J.: *Anales soc. españ. fis. quim.* **30**, 421 (1932); (quoted from Hengstenberg and Mark, *Naturwissenschaften* **20**, 539 (1932)).
- (18) FRIEDHEIM, E. A. H.: *J. Exptl. Med.* **54**, 207 (1931).
- (19) FRIEDHEIM, E. A. H.: *Compt. rend. soc. biol.* **112**, 1030, Mar. 18, 1933.
- (20) FRIEDHEIM, E. A. H.: *Biochem. Z.* **259**, 257 (1933).
- (21) FRIEDHEIM, E. A. H., AND MICHAELIS, L.: *J. Biol. Chem.* **91**, 355 (1931).
- (22) HABER, F., AND WILLSTÄTTER, R.: *Ber.* **64**, 2844 (1931).
- (23) HANTZSCH, A.: *Ber.* **49**, 511 (1916).
- (24) HANTZSCH, A., AND BURAWOY, A.: *Ber.* **65**, 1059 (1932).
- (25) HOFMANN, A. W.: *Ber.* **14**, 1497 (1881).
- (26) HOLIDAY, ENSOR R., AND STERN, KURT G.: *Ber.* **67**, 1352 (1934).
- (27) KENYON, JOSEPH, AND SUGDEN, SAMUEL: *J. Chem. Soc.* **1932**, 170.
- (28) KÖGL, FRITZ, AND POSTOWSKY, J. J.: *Ann.* **480**, 280 (1930).
- (30) KÖGL, FRITZ, AND TÖNNIS, B.: *Ann.* **497**, 265 (1932).
- (31) KUHN, RICH., AND WINTERSTEIN, ALFRED: *Ber.* **65**, 1737 (1932).
- (32) KUHN, RICH., AND WAGNER-JAUREGG, THEO.: *Ber.* **67**, 361 (1934).
- (33) KUHN, RICH., AND RUDY, HERMANN: *Ber.* **67**, 1298 (1934).
- (34) LANG, A., AND BIERICH, R.: *Z. physiol. Chem.* **223**, 180 (1934).
- (35) LASSEUR, A. PHILIPPE: G. et S. Thèse, Nancy, 1911.
- (36) LOEFFEL, ROBT. G.: *J. Biol. Chem.*, Proc. **109**, p. lvi (1935).
- (36a) MAZZA, F. P., AND STOLFI, G.: *Arch. sci. biol.* **16**, 1 (1931).
- (37) MICHAELIS, L.: *J. Am. Chem. Soc.* **53**, 2953 (1931).
- (38) MICHAELIS, L.: *J. Biol. Chem.* **92**, 211 (1931).

- (39) MICHAELIS, L.: J. Biol. Chem. **96**, 103 (1932).
- (40) MICHAELIS, L.: Biochem. Z. **250**, 564 (1932).
- (41) MICHAELIS, L., HILL, E. S., AND SCHUBERT, M. P.: Biochem. Z. **255**, 66 (1932).
- (42) MICHAELIS, L., AND HILL, E. S.: J. Am. Chem. Soc. **55**, 1481 (1933).
- (43) MICHAELIS, L., AND HILL, E. S.: J. Gen. Physiol. **16**, 859 (1933).
- (44) PICCARD, J.: Ber. **46**, 1843 (1913).
- (45) PICCARD, J., AND DARDEL, J. H.: Ber. **56**, 2253 (1923).
- (46) SCHLENK, W.: Ann. **363**, 313 (1908); **368**, 277 (1909).
- (47) SHAFFER, PHILIP A.: J. Biol. Chem., Proc. **105**, p. lxxviii (1934).
- (48) STERN, KURT G.: Biochem. J. **28**, 949 (1934).
- (49) STERN, KURT G., AND HOLIDAY, ENSOR R.: Ber. **67**, 1104, 1442 (1934).
- (50) SULLIVAN, M. X., COHEN, B., AND CLARK, W. M.: U. S. Pub. Health Repts. **38**, 1669 (1923).
- (51) TAYLOR, N. W., AND LEWIS, G. N.: Proc. Nat. Acad. Sci. **11**, 456 (1925).
- (52) THEORELL, HUGO: Biochem. Z. **275**, 344 (1935).
- (53) WAGNER-JAUREGG, THEO., AND RUSKA, H.: Ber. **66**, 1298 (1933).
- (54) WARBURG, OTTO, AND CHRISTIAN, W.: Biochem. Z. **266**, 377 (1933).
- (55) WEITZ, E., AND LUDWIG, RICH.: Ber. **55**, 395 (1922).
- (56) WEITZ, E., KÖNIG, TH., AND WISTINGHAUSEN, L.: Ber. **57**, 153 (1924).
- (57) WEITZ, E., AND FISCHER, K.: Ber. **59**, 432 (1926).
- (58) WEITZ, E., AND SCHWECHTEN, H. W.: Ber. **59**, 2307 (1926).
- (59) WEITZ, E., AND MEITZNER, E.: Ber. **64**, 2909 (1931).
- (60) WEITZ, E.: Z. Elektrochem. **34**, 538 (1928).
- (61) WILLSTÄTTER, RICH., AND KALB, L.: Ber. **37**, 3761 (1904).
- (62) WILLSTÄTTER, RICH., AND PICCARD, J.: Ber. **41**, 1458 (1908).
- (63) WREDE, F.: Z. Hyg. Infektionskrankh. **111**, 90 (1930).
- (64) WREDE, F., AND STRACK, E.: Z. physiol. Chem. **140**, 1 (1924); **142**, 103 (1925); **177**, 177 (1928); **181**, 58 (1929).
- (65) WREDE, F., AND STRACK, E.: Ber. **62**, 2051 (1929).

ACIDS, SALTS, AND BASES¹

NIELS BJERRUM

Chemical Laboratory of the Royal Veterinary and Agricultural College, Copenhagen, Denmark

(Translated from the Danish by Mary L. Kilpatrick, Laboratory of Chemistry, University of Pennsylvania, Philadelphia, Pa.)

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It is not the purpose of this article to present a complete account of the way in which the concepts of acid, salt, and base have been developed in the course of time. Rather it is its purpose to give a description of the developments these concepts have undergone during the last twenty years, developments to which J. N. Brönsted (8) in particular has made important contributions. In the presentation an effort is made to emphasize the continuity between the old and the new conceptions, and to show how it is possible to use what is good in the new development without giving up the good in the old. It is my hope to help to bring about the more common use and recognition of the new ideas, not only in scientific work, but also in elementary teaching.

ACIDS

Let us begin with the concept of an acid. About 1900, in elementary teaching an acid was described as a hydrogen compound which tasted sour and in aqueous solution colored litmus red (reacted acid). In somewhat more advanced teaching, this description was elaborated by defining an acid as a hydrogen compound which could split off hydrogen ions. By and large, I believe that this presentation is still valid.

Just after the coming out of the ionic theory, there was an inclination to stipulate that the hydrogen compound should be separated into ions before it could be called an acid. Thus it was said that hydrogen chloride was not an acid until it was dissolved in water. From my student days I remember how Biilmann, then an assistant, came up to a group of young students one day and raised the question as to whether hydrogen sulfide was really an acid. At that time it was a little puzzling, the question of whether the hydrogen compound itself should be called an acid, or whether only the part separated into hydrogen ions and anions should have that

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name. The point was soon cleared up, however, at least among the better informed. The power to split off hydrogen ions became the official criterion for an acid. It is quite another matter that the quantity of hydrogen ions in the aqueous solution of the substance in question tells whether the substance is a stronger or a weaker acid.

It has no doubt always been considered self-evident that not only neutral molecules (like hydrogen chloride and acetic acid), but also anions (like the bicarbonate ion, HCO_3^- , and the primary and secondary phosphate ions, H_2PO_4^- and HPO_4^{--}) should be regarded as acids. In the acid salts which contain these acids one has to do with substances which are at the same time acids and salts.

On the other hand, it is only recently that cations which can split off hydrogen ions have been regarded as acids. Of course many people have long realized that the so-called hydrolysis of ammonium salts results from the reaction



and that accordingly the weakly acid character of aqueous solutions of ammonium salts is due to the power of the ammonium ion to split off a hydrogen ion (14, 18), but to Brönsted (8) belongs the honor of having drawn from that fact the conclusion that we should regard the ammonium ion as an acid.

Brönsted designates uncharged acids (HCl , CH_3COOH) as neutral acids, negatively charged acids (HCO_3^-) as anion acids, and positively charged acids (NH_4^+) as cation acids.

Using Brönsted's extension of the name "acid" we must reckon as acids not only the ammonium ion and the alkyl substituted ammonium ions in the salts of the amines, but also the hydrated metal ions (aquo ions) which many salts form in aqueous solution, for example, $\text{Cr}(\text{H}_2\text{O})_6^{+++}$, $\text{Al}(\text{H}_2\text{O})_6^{+++}$, $\text{Cu}(\text{H}_2\text{O})_4^{++}$, and so on. As Pfeiffer (18) pointed out in 1906, these aquo ions can split off hydrogen ions, forming the so-called hydroxo compounds. Thus by the splitting-off of hydrogen ions from the hexaaquochromic ion there can be formed the monohydroxo ion, $\text{Cr}(\text{H}_2\text{O})_5(\text{OH})^{++}$, the dihydroxo ion, $\text{Cr}(\text{H}_2\text{O})_4(\text{OH})_2^+$, chromic hydroxide, $\text{Cr}(\text{H}_2\text{O})_3(\text{OH})_3$, and the chromite ion, $\text{Cr}(\text{H}_2\text{O})_2(\text{OH})_4^-$. The basic compounds which are formed upon the hydrolysis of salts of metals are very often (but by no means always) such hydroxo compounds, formed by the simple splitting-off of hydrogen ions from aquo ions. By regarding the hydrated metal ions as acids, as Brönsted does, one obtains a pedagogically useful, simple explanation of the acid reaction of these salts (their hydrolysis).

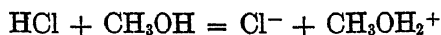
The advantage of Brönsted's extended use of the name "acid" is easy to see. Our mode of expression is thereby brought into closer agreement

with the definition of an acid, and is in many cases made simpler and more comprehensible. The extension does not seem to have encountered much opposition. On the contrary, with hindsight it appears so obvious that one involuntarily asks one's self, "How is it that chemists didn't hit upon it sooner?" The extension cannot be explained as the result of new, previously unknown facts. No, the thing which prevented chemists from applying their own definition of an acid to the cation acids is certainly the fact that they have unconsciously required that an acid combine with metal hydroxides to form a salt and water. This requirement the cation acids do not meet. Thus ammonium chloride and sodium hydroxide form not only salt and water, but also ammonia. This requirement is certainly not contained in the official definition of an acid, but has existed and still exists, more or less unrecognized, in chemists' ideas of an acid. It possesses the rights of age. In calling the ammonium ion and ammonium salts acids, one must refuse to recognize this requirement.

My early work with aquo salts and their hydrolysis (2), and with the constitution of the amino acids (3), made it especially easy for me to see the usefulness of Brönsted's extension of the acid concept. And I believe that I may take credit for having seen, even earlier than the originator, the applicability of the new use of the word to the hydrogen ion in aqueous solution. By that time it had become a commonly accepted idea that the hydrogen ion, H^+ , is not found free in its solutions, but is always present in solvated form, for example, as H_3O^+ (hydroxonium ion) in aqueous solution. This idea, which can be traced back to the work of Franklin (12), Goldschmidt (15), and Fitzgerald and Lapworth (11) received strong support shortly before 1923 in a paper by Fajans (10). In my work on polybasic acids (4) I start out from the supposition that the hydrogen ion exists in aqueous solution as hydroxonium ion, and in agreement with Brönsted's concept, I regard the hydroxonium ion as a tribasic acid and discuss the values of its three dissociation constants.

While the hydrogen ion is present in water as H_3O^+ (hydroxonium ion), in methyl alcohol it is present as $CH_3OH_2^+$ (methyloxonium ion), in liquid ammonia as NH_4^+ (ammonium ion), and so on. Chemists speaking of hydrogen ions in daily conversation practically always have in mind these solvated hydrogen ions. This is a somewhat dangerous use of words,—especially dangerous when it is necessary to distinguish between free and solvated hydrogen ions. If it is decided to call the free hydrogen ion a hydrogen kernel or proton, the term "hydrogen ion" can still be used for the solvated hydrogen kernel. But I regard it as distinctly more practical to introduce a special common name for these solvated hydrogen ions, and I propose to call them "lyonium" ions (the Greek word "lyo," to dissolve, is used in the prefix of the terms "lyophilic" and "lyophobic" colloids).

When an acid ionizes in a medium, its hydrogen ion is given to the solvent with formation of a lyonium ion. For example,



In this reaction the original acid (hydrogen chloride) disappears, but there is formed in its stead a new acid, i.e., the lyonium ion (in our example, the methyloxonium ion). In solutions of strongly dissociated acids we have in fact no longer the original acid, but only the lyonium-ion acid.

Summarizing, it can be said that the new Brönsted phase in the development of the concept of an acid does not bring any change in the commonly used definition of an acid. It merely requires that the definition be taken quite literally, just as it is stated.

SALTS

While the concept of an acid may now be said to have found rational demarcation, the salt concept still suffers from an irrational ambiguity.

We have all been brought up to regard as salts those substances which are formed upon neutralization of acids by bases, and whose formulas can be derived from those of acids (neutral acids) upon replacing the hydrogen atoms of the acid with metal atoms, or with certain compound radicals which behave like metal atoms.

By the side of this official concept, as it might be called, another use of the word "salt" has quietly appeared. Thus it is often said that mercuric chloride and mercuric cyanide are not salt-like substances, there is doubt as to the salt-like nature of anhydrous aluminum chloride, etc. Behind these statements lies the thought that only ionized substances should be spoken of as salt-like. In the same way an effort is made to avoid calling the alkyl derivatives of acids alkyl salts. The term "ester" furnishes an excellent, noncommittal name for them.

It is easy to see the danger of using the word "salt" simultaneously with two different meanings, one which lays emphasis upon the *composition*, metal plus acid residue, and another which lays emphasis upon the *properties* which result from ionization. We should try to agree to use the word "salt" for one of these meanings only. This is surely most easily accomplished if at the same time we introduce a new name for the other meaning.

I believe that it will be most practical to keep the word "salt" for the substances which possess ionic structure, i.e., which are built up from and still contain ions. As the new name for the derivatives of neutral acids in general, without consideration of their ionization, I propose the term "acidate." This word seems to me to serve excellently as a common name for ionized salts, complex metal compounds, and organic esters, in the same way that the word "sulfate" (chloride, etc.) serves as a common name

for substances of all these types derived from sulfuric acid (hydrochloric acid, etc.). If this differentiation between salts and acidates is adopted, it can be said that mercuric cyanide and ethyl acetate are acidates, but not salts. Dry hydrogen chloride is not a salt, but upon dissolving in water it forms a salt solution, since chloride and hydroxonium ions (i.e., a lyonium salt) are formed. Other strong acids behave in the same way. In aqueous solution a weak acid like acetic acid is a mixture of a small amount of ions (a lyonium salt) and a great quantity of undissociated non-salt. Alum is both a double acidate and a double salt. On the other hand, potassium ferrocyanide is a double acidate but not a double salt.

Salt and acidate

Since all anions can combine with the hydrogen ion to form acids, every salt is of necessity an acidate. The salts form a subdivision of the larger class of acidates. The term "salt" is therefore more restrictive than the term "acidate," and it is generally easier to decide whether or not a substance is an acidate, than it is to decide whether or not it is a salt. A knowledge of composition alone as a rule enables one to decide whether a substance is an acidate of a given acid or not. On the other hand, it is frequently difficult to establish the fact that a substance is composed of ions, i.e., that it has the nature of a salt. If the substance is soluble, we have in the power to conduct electricity an excellent criterion for ions. But in the solid state we have no such reliable test, and at the present time doubt exists in many cases. At ordinary temperatures, are the silver halides salts as defined above, or not? Opinion on this point is divided.

Salt and ion

The term "salt" plays in the nomenclature of substances a part similar to that which the term "ion" plays in the nomenclature of molecules. An ion cannot be obtained in the pure state as a substance. If one wishes an ion in the form of a substance which can be collected and weighed, bought and sold, one must take another ion at the same time, i.e., one must deal with a salt.

Salt and electrolyte

The introduction of the new usage does not mean that salt and electrolyte become two names for one and the same thing. An electrolyte is a substance which is dissociated into ions to a demonstrable, but to any arbitrarily small, degree. A salt on the other hand is a substance which is entirely composed of ions.

Acidate and derivative

The term "derivative" is closely related to the term "acidate." Derivatives are frequently understood to be substances derived from hydrogen

compounds upon replacement of hydrogen by something else, and since formally all hydrogen compounds may be regarded as acids (although sometimes extremely weak), all such derivatives are acidates. The term "derivative" is, however, also used in a more inclusive way. Thus acetamide may be derived from acetic acid upon replacement of the *hydroxyl* group by the amino group. It is a derivative of acetic acid, but not an acidate of it.

Salt and acid

That a substance is an acid has nothing to do with the fact that it is possibly a salt as well. A substance which is an acid is not necessarily a salt, but it may be a salt in the same way that a substance which is an acid may also be an alcohol (an oxy acid). Thus the ammonium salts and the so-called acid salts are at the same time acids and salts. Nevertheless, there is always a certain relationship between acid and salt in that those acids which are not themselves ions become ions upon neutralization (i.e., upon splitting off hydrogen ions).

For the understanding of the significance of the new concept of a salt it is very helpful to recall that our chemical substances can be divided quite naturally into three large groups, for each of which there are characteristic criteria: (1) metals, which consist of positive ions together with negative electrons. (2) Salts, which consist of positive and negative ions. (3) The remaining nonmetallic and nonsalt-like substances, which consist of neutral molecules.

Summary

In order to obtain a clear and unambiguous nomenclature, it is proposed to call all substances which can be derived from neutral acids by replacement of hydrogen with metal atoms, or with other radicals, acidates. Many of the acidates, but by no means all, belong to the great class of substances which are characterized by being constructed of ions. It is proposed to restrict the use of the term "salt" to these ionized substances.

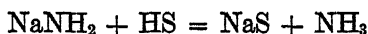
BASES

The use of the word "base" is at the present time particularly vague and ambiguous. We have all been brought up to think of a base as a hydroxyl compound which splits off hydroxyl ions in aqueous solution. Back of this definition lies the idea that a base shall be a substance which, in the first place, can neutralize an acid solution, i.e., rob it of its acid properties, and in the second place, upon neutralization combine with the acid to form a salt (or more generally an acidate) and water. But whether we consider the matter logically or empirically, the power to neutralize and the power to form an acidate and water are not inseparably linked. Since in general

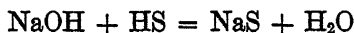
there has been a more or less instinctive tendency to regard the power to neutralize an acid as the more important, there have been constant efforts to extend the concept of a base so as to include, in addition to the hydroxyl compounds, other substances which can neutralize acids.

Thus many chemists have continued to call ammonia and the amines bases, as was done long ago. I can mention Goldschmidt (14) and Fitzgerald and Lapworth (11), for example. Even water and other solvents which can combine with the hydrogen ion to form lyonium ions are called bases by Fitzgerald and Lapworth. Pfeiffer (18) was the first to notice that many metal hydroxides—the hydroxo compounds—can add acids and thereby form aquo salts without splitting off water; he decided for this reason to call the hydroxo compounds pseudo bases. At almost the same time Werner (20) made a distinction between anhydro bases and aquo bases, according as the salt formation takes place without or with the formation of water.

The concept of a base was extended in another way by Franklin (13). Through his work with the solvent liquid ammonia he was led to call metal amides like NaNH_2 ammonio bases. For in liquid ammonia the metal amides react with acids to form salt plus solvent according to the equation



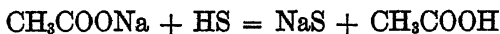
i.e., in a way quite analogous to the formation of a salt from a metal hydroxide and acid in aqueous solution



If one generalizes Franklin's idea, in alcoholic solution the alcoholates or alkylates, as I prefer to call them, are to be regarded as bases



and similarly in glacial acetic acid the acetates should be regarded as bases



This generalization, however, leads very easily to the masking of what is the essential property of a base. For example, continuing as before one is easily brought to look upon sodium chloride dissolved in dry hydrogen chloride as just as good a base as sodium hydroxide in water.

In 1923 Brönsted (8) attempted to extend the concept of a base in a different way. He advocated the use of the term "base" for molecules which can neutralize acids, and entirely disregarded what is formed in the neutralization. When an acid is neutralized, its hydrogen ion is removed,

and so Brönsted arrived at the simple conclusion that a base should be defined as a molecule which can combine with the hydrogen ion. Through this extended definition Brönsted evaded a number of difficulties. Among the bases he included all the molecules which in any way have previously been counted as bases.

The list in table 1 gives some idea of the molecules which are bases according to Brönsted's definition. Many of them are ions. All the salt-like substances which contain these ions are to be regarded as bases, and are accordingly included in the table.

Brönsted's definition, like Franklin's generalization, causes every anion (and so every salt) to be classed as a base. For we know no anion which cannot form undissociated acid molecules with the hydrogen ion. The perchlorate ion possesses this power to the smallest extent, and is therefore the weakest known anion base.

TABLE 1
Bases according to J. N. Brönsted

MOLECULES OR IONS	SALT-LIKE SUBSTANCES
NH ₃ and the amines	
H ₂ O and the alcohols	
Hydroxo compounds (nonsalt-like metal hydroxides)	
C ₂ H ₅ O ⁻ (C _n H _{2n+1} O ⁻)	Ethylates (alkylates)
OH ⁻ , O ²⁻	Hydroxides and oxides
HCO ₃ ⁻ , CO ₃ ²⁻	Bicarbonates and carbonates
CH ₃ COO ⁻	Acetates
ClO ₄ ⁻	Perchlorates

The useful feature of Brönsted's definition is that it points out the basic nature of the substance in question without reference to a solvent, and at once indicates a way to measure basic strength by measuring the power of the base to combine with the hydrogen ion.

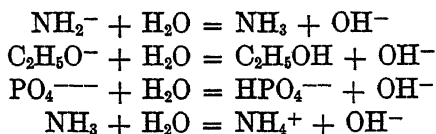
Quite rightly Brönsted is much pleased with his new and elegant definition of a base. In his easily understood enthusiasm, however, he has been hardly sufficiently aware of the unique position which the hydroxides occupy among bases, and which is the reason that the name "base" was previously reserved for these substances. If we follow Brönsted and use the name "base" not only for sodium hydroxide but also for sodium carbonate and sodium acetate, substances which all of us have actually employed to neutralize acid solutions, we shall need a new term for the substances which, like hydroxides and oxides in aqueous solution, alkylates in alcoholic solution, and acetates in glacial acetic acid, unite with acids to

form acidates (salts) plus solvent. In preparative chemistry this is a very important property. In distinction to these bases, other bases (bases in the extended sense) form upon neutralization an acidate (salt) and an acid different from the solvent. Thus carbonates in aqueous solution give carbonic acid (carbon dioxide), acetates in aqueous solution give acetic acid, and so on.

The bases to which we are thinking of giving a special name are the solvents' own acidates. I propose to call them "lyates." The ion base characteristic of these substances, which consists of the solvent minus the hydrogen ion, may very well be called "the lyate ion." Just as the concentration of the lyonium ion is customarily written c_H , the concentration of the lyate ion may well be written c_{-H} .

The special character of the lyates and the lyate ions among bases is evident not only in preparative work, where the lyates react with acids to form pure acidate solutions, but is also important in applications of the mass action equations to ionic equilibria in dilute solution. This last is due to the fact that the lyates, as acidates of the solvent, are derived from an acid which in dilute solution acts at nearly constant concentration and active mass.

One more property may be mentioned as a characteristic of lyate ions. In a solvent of acid nature any strong base will react with the solvent to form lyate ion. For example,

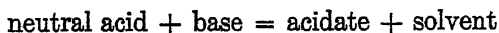


If the base is sufficiently strong the reaction will be practically complete. So in an acid solvent bases which are appreciably stronger than the solvent's lyate ion cannot exist. Similarly, in a basic medium which is capable of forming lyonium ions, acid molecules which are appreciably stronger acids than the lyonium ion do not exist, for these acids will react with the solvent to form lyonium ion.

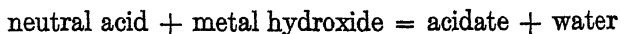
The adoption of Brönsted's extended definition of a base means that the old classical equation



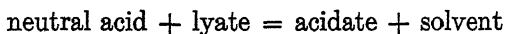
must be abandoned. Nor can the somewhat modernized version of this equation



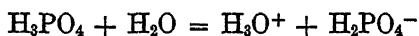
be kept. It is, however, not necessary to give up the equation altogether. We can keep the equation if for *base* we substitute *metal hydroxide*



or more generally,

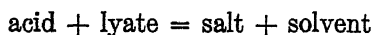


When a neutral acid is dissolved in a basic medium, as already mentioned, there is formed a smaller or greater amount of lyonium salt. For example,

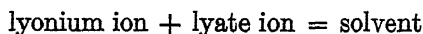


The lyonium salt formed is neutralized by lyates, just as the original acid is, with formation of acidate and solvent. It does not as a rule do any harm, therefore, to use the word "acid" to represent the sum of the actual neutral acid (HS) and its lyonium salt (in aqueous solution $\text{H}_3\text{O}^+ + \text{S}^-$) present in the solution. On the contrary, this nomenclature is to be recommended as suitable and convenient in many instances.

If a solution of a strong base (the base being completely transformed to lyate salt) neutralizes a solution of a strong acid (the acid being present wholly as lyonium salt), the process of neutralization is of an especially simple character. When the equation



is rewritten in ionic form and simplified, we get for the process of neutralization



This takes on for aqueous solutions the well-known form



It follows from these equations that dilute solutions of all strong acids and strong bases have the same heat of neutralization in the same amphoteric solvent.

The trouble with the old concept of a base comes from the fact that we have tried to kill two birds with one stone, and combine the concepts of base and lyate. By separating the two concepts we succeed in preserving the good in them both. The lyates are a subdivision of the bases. They occupy a unique position in synthetic and formal chemistry.

I regard it as an advantage that the name "lyate" as defined here includes both oxides and hydroxides without reference to the greater or

smaller water content of these compounds. I have always felt it pedagogically unwise to emphasize the hydroxyl compounds, which are often known only on paper (for example, $\text{Fe}(\text{OH})_3$), at the expense of their partial or complete anhydrides ($\text{Fe}_2\text{O}_3 \cdot \text{H}_2\text{O}$, Fe_2O_3).

As a matter of fact, the lyate concept is more closely related to the old official concept of a base than is Brönsted's extended concept. There is therefore some reason for continuing to use the word "base" for the substances which in this paper are called lyates. In that event it would be necessary to coin a new word for Brönsted's bases in the extended sense. The term "antacid" might be suggested. But after long hesitation I have finally come to the conclusion that it is best to try to push through the use of the term "base" for the extended concept, and introduce the new name "lyate" for the acidates of the solvent.

Summary

It is probably satisfactory, in preparatory school, to describe bases as substances which impart a basic reaction (taste, litmus) to water, and which can neutralize (quench) the acid properties of acid solutions. Among the bases should be reckoned, besides the hydroxides of the alkalis and other metals, the oxides of the metals, and ammonia, and the carbonates. In addition it should be pointed out that the hydroxides and oxides are remarkable in that they combine with an acid to give an acidate and water, and that ammonia combines with an acid to give an acidate with no formation of water. To the more advanced student Brönsted's definition of a base should be taught, and the lyate concept should be formulated to cover nonaqueous solutions.

ACID, NEUTRAL, AND BASIC REACTION

In aqueous solution distinction is made between acid, basic, and neutral reaction according as the hydrogen ions (more exactly expressed, the hydroxonium ions) or the hydroxyl ions, or neither, preponderate to a marked degree. The new extension of the concepts of acid and base causes no change here. The reaction of the solution can still be stated quantitatively in terms of the hydrogen-ion concentration, or, to use the system devised in 1909 by Sørensen (19), in terms of the hydrogen-ion exponent, defined as the negative logarithm of the hydrogen-ion concentration, $\text{pH} = -\log c_{\text{H}}$. Since 1909 the only important changes which have taken place in stating the reaction of aqueous solutions have been: first, to define the hydrogen-ion exponent pH in a new way, according to which it is not exactly equal to $-\log c_{\text{H}}$, but is more easily calculated from electrometric determinations (9), and secondly, to introduce as a measure of the reaction of a solution the hydrogen-ion activity a_{H} , measured on a scale which

for very dilute solutions coincides (or almost coincides) with hydrogen-ion concentration (5,7). This requires furthermore the use of $p_aH = -\log a_H$ in place of pH .

The rational use of the concepts of acid, basic, and neutral reaction in a nonaqueous solution is dependent upon the ability of the medium to take up and give off hydrogen ions.

In amphoteric media which, like water, can form both lyonium and lyate ions, it is possible to use the concentration of these ions to distinguish between acid, basic, and neutral solutions, just as in water. On the other hand, if the medium lacks acid character and so cannot form lyate ions, one cannot speak of basic solutions in the same sense as in water. If the medium lacks basic character and consequently cannot form lyonium ions, one cannot speak of acid solutions in the same sense as in water. And finally if the medium is neither acid nor basic, and so can form neither lyate nor lyonium ions, one can speak of neither acid nor basic solutions in the same sense as in water.

The hydrogen-ion exponent pH , defined as $-\log c_H$ (and p_aH defined as $-\log a_H$, where a_H is the hydrogen-ion activity, measured on a scale which at infinite dilution coincides with lyonium-ion concentration), has a definite value only in basic media which can form lyonium ions. There is, to be sure, nothing to prevent the determination of *relative* hydrogen-ion activities in nonbasic media. But the hydrogen-ion activity cannot be given on a lyonium-ion scale. It must be given on the scale of hydrogen-ion activity established for aqueous solutions. The hydrogen-ion activity A defined in this manner, or rather its negative logarithm pA , was proposed by Michaelis and Mizutani (17) as a measure of the degree of acidity of all nonaqueous solutions. Linderström-Lang (16) has agreed to this proposal. Brönsted (8) has suggested calling the hydrogen-ion activity measured on the water scale (A) the acidity of the solution. Correspondingly pA might be called the acidity exponent.

For nonaqueous solutions which can form lyonium ions it is possible to use both c_H and A , both pH and pA , as a measure of the degree of acidity. A great deal can be advanced in support of the use of the different quantities, and probably fields will be found in which each is most convenient. I shall not go into this question at the present time, however.

The extent and position of the scale of reaction

Where only dilute solutions (at the most 1 normal) are concerned, the pH scale in water has a rather definite length. The hydrogen-ion concentration in even the most acid solution (1 normal in acid) cannot be greater than 1, and the pH accordingly not less than 0. On the other hand, the hydrogen-ion concentration in the most strongly basic solution (1 normal

in base) cannot be less than the dissociation constant of water, about 10^{-14} , and consequently the pH cannot be greater than $-\log K = 14$, approximately. There is naturally a close connection between the limited extent of the reaction scale in water and the fact that acids and bases whose strength exceeds certain limits do not exist as such in aqueous solution. Acids like hydrochloric acid, whose strength exceeds that of the hydroxonium ion, will form hydroxonium ion upon dissolving in water. And bases like sodium amide, whose strength exceeds that of the hydroxyl ion, will form hydroxyl ions in water. Since the substances are thereby transformed, and are present only in the transformed state, their greater strength is not manifest in the reaction of the solution.

Since ethyl alcohol is both an acid and a basic medium, and its dissociation constant is of the order of magnitude of 10^{-20} , the pH reaction scale

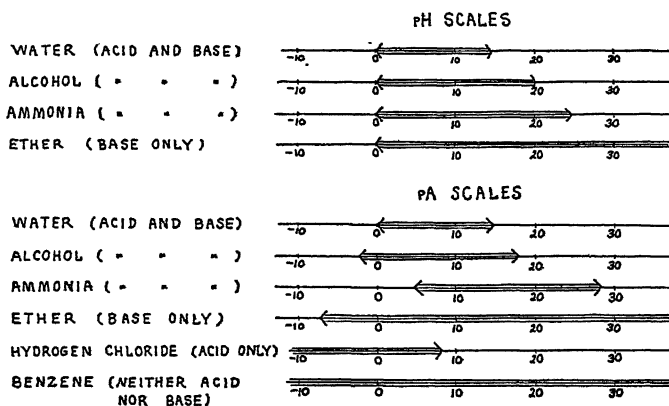


FIG. 1. POSITION OF THE REACTION SCALES IN TYPICAL SOLVENTS

in ethyl alcohol goes from 0 to 20. On the pA scale the most strongly acid solutions in alcohol do not lie at $pA = 0$, but at $pA = -2.5$, and since the pA scale has the same extent as the pH scale, the most strongly basic solutions lie at $pA = 17.5$ in ethyl alcohol. The pA scale therefore extends from -2.5 to 17.5 . The value of pA for the most strongly acid solutions (the end of the pA scale on the acid side) is determined primarily, although not exclusively, by the basic strength of the medium. If the medium is a stronger base than water, the pA scale usually begins at positive values. If on the other hand the medium is a weaker base than water, the pA scale usually begins at negative values. In alcohol the pA scale begins on the negative side, and in liquid ammonia on the positive (see figure 1).

In the case of a medium which can take up but cannot give off hydrogen ions (for example, ether $(C_2H_5)_2O$), both the pH and pA scales are without a limit on the basic side.

In the case of a medium which cannot take up hydrogen ions, only the pA scale can be used, and this is unlimited on the acid side. In a medium which cannot take up but can give off hydrogen ions the pA scale is without a limit on the acid side, but limited on the basic. As an example of such a medium hydrogen chloride may be mentioned. If hydrogen chloride should be found upon closer examination to possess some slight power to take up hydrogen ions, the pA scale for this solvent would not be infinitely long on the acid side, but would merely extend far out on this side.

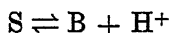
If the medium can neither take up nor give off hydrogen ions (for example, benzene), the pA scale is unlimited on both sides.

In figure 1 is given a diagrammatic representation of the scale of reaction in a number of typical solvents.

THE MEASURE OF ACID AND BASIC STRENGTH

The commonly used measure of the strength of an acid is its dissociation constant. As is well known, the dissociation constant is equal to the hydrogen-ion concentration (lyonium-ion concentration) in a half-neutralized acid solution. (By a half-neutralized acid solution is meant a solution which contains just as many molecules of the acid itself as of the acid minus hydrogen ion.) As a measure of the acid strength one can use, in place of the hydrogen-ion concentration, any other of the numbers which may be employed to give the reaction of the half-neutralized solution (*A*, pH, pA). Using pH one obtains the pK value of the acid (its dissociation exponent). In general it is most practical to use the same number as that selected for stating the reaction of a solution.

When an acid molecule (*S*) splits off its hydrogen ion, there is formed an acid residue (*B*). The acid residue, as Brönsted quite rightly emphasizes, must always be a base, in that it can combine with hydrogen ion to form an acid



Brönsted calls acids and bases which stand in this mutual relationship to each other "corresponding." It is easy to understand why chemists in the past have not been aware of the correspondence between acids and bases. In the first place, correspondence appears only when Brönsted's extended concept of acids and bases is used. Moreover, the base corresponding to a fairly strong acid is a very weak base, and conversely the acid corresponding to a fairly strong base is a very weak acid. Only when one understands by *acids* and *bases* not only the substances which give to water a decidedly acid or basic reaction, but rather all substances which have the power to split off or take up hydrogen ions, does the correspondence emerge clearly.

As a measure of the strength of bases Brönsted (8) has proposed to use the reciprocal of the dissociation constant of the corresponding acid. It is surely more practical, however, to use the same value for an acid and for its corresponding base, i.e., to use as a measure of strength for both acids and bases the reaction of the half-neutralized solution. Both the strength of the ammonium ion as an acid and the strength of ammonia as a base can be measured by the number which gives the reaction of a solution in which the ammonium ion and ammonia are present at the same concentration. Using the reciprocals for bases merely increases the number of quantities to be remembered and tabulated, and makes more difficult the grasp of the relationship between the reaction and the extent of neutralization in the case of bases. I grant that people are going to be reluctant to express basic strength by a number which increases with decreasing basic strength. But just as we have become accustomed to expressing the degree of acidity in pH values, which undeniably increase with decreasing acidity, we can surely become accustomed to expressing basic strength by a number which increases as basic properties decrease.

In aqueous solution one can use as a measure of the reaction of the half-neutralized solution the lyonium-ion concentration (c_H) or the hydrogen-ion exponent (pH). In nonaqueous, basic media one can use, in addition to these quantities, the acidity A or its negative logarithm, the acidity exponent pA. On the other hand, in nonaqueous, nonbasic media one can use only the last two, the acidity and the acidity exponent (A and pA).

Whether the one or the other of these possible measures is used, care must be taken that the same measure is employed throughout the work in a given solvent. The value of the strength of an acid depends on the medium, whatever scale of reaction is used. It is not even to be expected that the same sequence of acid strength (except very approximately) will be found upon comparing acids in different media. In a paper on the distribution coefficients of ions between different media, Larsson and I (6) have tried to work out the theory of the variation of acid strength with medium, but I shall not go into the matter at this time.

Since free hydrogen ions (hydrogen kernels, protons) are not found at finite, determinable concentrations in any of our solutions, it is not possible to determine the absolute dissociation constants or absolute strengths of acids and bases. The strength of the acid (base) is given in relation to the strength of the lyonium ion (the medium itself) when the strength is stated in terms of the lyonium-ion concentration of the half-neutralized solution. And when the acidity scale is employed, the strength of the acid (base) is compared with the strength of the hydroxonium ion (water). It must not be forgotten, however, that the specific properties of the medium, especially the dielectric constant, have a marked and very varied effect upon the

strength of acids (bases), so that even in the case where the strength is always compared with that of the hydroxonium ion (water), different values may be obtained in different media.

Summary

As a measure of the strength of an acid and the strength of the corresponding base in a given medium, one of the quantities which may be employed to give the reaction of their half-neutralized solution should be used. The choice lies between the lyonium-ion concentration c_H , the acidity A , the hydrogen-ion exponent pH , and the acidity exponent pA . The worker should always select the same quantity which he employs in stating the reaction of his solutions. None of these quantities gives numerical values of acid and basic strength which are independent of the medium, or even proportional to one another in different media (or which in the case of the logarithmic quantities yield the same difference in different media).

THE THEORY OF TITRATION

The theory of titration is not changed by the introduction of the new concepts of acid and base from the form in which I gave it many years ago (1), but because of its close relation to the problems discussed in this paper, I shall make a few remarks about it here, especially about its application to nonaqueous solutions.

The theory of titration furnishes a means of calculating the error made in titrating a solution of one or several acids or bases to the change point of some given indicator. For aqueous solutions the procedure is as follows: The position of the change point of the indicator (p_T) is marked on the scale of reaction, as are the points which give the strengths of the acids and bases present ($p_1, p_2, p_3, \dots$). The errors which arise depend altogether upon the position of p_T relative to the points $p_1, p_2, p_3, \dots$, and relative to the ends of the scale of reaction (0 and 14). Sharp change of color and consequent accurate titration result when p_T lies far from all these points. If p_T is kept at a distance of at least three units from a p , the error arising from the presence of the acid (base) is less than 0.1 per cent of the amount of the acid (base) in question. If d is the distance between p_T and p , the error is less than 10^{-d} of the amount of the acid (base) corresponding to the p . If the distance between p_T and the ends of the scale is at least four units, the so-called hydrogen- and hydroxyl-ion errors are at most 0.01 cc. of 1 normal titration liquid when the final volume of solution is 100 cc. Generally speaking, this error is at most $v \times 10^{-d}$ cc. of normal titration liquid (v is the final volume and d the distance between p_T and the nearer end of the scale (0 or 14).

When the procedure is to be transferred to nonaqueous solutions, the only thing to be changed is the ends of the scale, which no longer lie at 0 and 14, but at the numbers which give the reaction of solutions 1 normal in lyonium ion and 1 normal in lyate ion respectively. If the medium does not form lyonium ions, or does not form lyate ions, the scale is unlimited on the corresponding side, and the error arising from too close approach to the end of the scale on this side disappears. In benzene and other media where the scale of reaction is unlimited on both sides, one has to prevent only the too close approach of the titration exponent p_T to the p 's corresponding to the acids and bases present.

SUMMARY

I hope that I have succeeded in describing the manner in which the recent extension of the concepts of acid, base, and salt, primarily through Brönsted's useful and clarifying work, has progressed to a point where it will be desirable to introduce the new viewpoint and the new definitions into the elementary teaching of chemistry.

REFERENCES

- (1) BJERRUM, N.: Die Theorie der alkalimetrischen und azidimetrischen Titrierungen, Enke, Stuttgart (1914) (also in Sammlung chem. u. chem.-tech. Vorträge **21**, 1 (1914)); Z. anal. Chem. **56**, 87 (1917).
- (2) BJERRUM, N.: Studier over basiske Kromiforbindelser, Prior, Copenhagen (1908); Z. physik. Chem. **73**, 725 (1910); Z. anorg. allgem. Chem. **118**, 143, 158 (1921).
- (3) BJERRUM, N.: Z. physik. Chem. **104**, 147 (1923).
- (4) BJERRUM, N.: Z. physik. Chem. **106**, 219 (1923).
- (5) BJERRUM, N., AND GJALDBÆK, J. K.: Landbohøjskolens Aarsskrift, p. 69. Copenhagen (1919).
- (6) BJERRUM, N., AND LARSSON, E.: Z. physik. Chem. **127**, 358 (1927).
- (7) BJERRUM, N., AND UNMACK, A.: Kgl. Danske Videnskab. Selskab Math.-fys. Medd. **9**, No. 1, 82 (1929).
- (8) BRÖNSTED, J. N.: Rec. trav. chim. **42**, 718 (1923); J. Phys. Chem. **30**, 777 (1926); Chem. Rev. **5**, 232 (1928); Ber. **61**, 2049 (1928); Z. physik. Chem. **143A**, 229 (1929); Z. angew. Chem. **43**, 229 (1930); Z. physik. Chem. **169A**, 52 (1934).
- (9) CLARK, W. M.: The Determination of Hydrogen Ions, 2nd edition, p. 276, 3rd edition, p. 477. The Williams & Wilkins Co., Baltimore (1922 and 1928, respectively).
- (10) FAJANS, K.: Naturwissenschaften **9**, 734 (1921); Z. Physik **23**, 31 (1924).
- (11) FITZGERALD, E., AND LAPWORTH, A.: J. Chem. Soc. **93**, 2117 (1908).
- (12) FRANKLIN, E. C.: Z. anorg. allgem. Chem. **46**, 3 (1905).
- (13) FRANKLIN, E. C.: Am. Chem. J. **23**, 304 (1900); J. Am. Chem. Soc. **27**, 820 (1905); Z. anorg. allgem. Chem. **46**, 1 (1905).
- (14) GOLDSCHMIDT, H.: Z. physik. Chem. **29**, 89 (1899); **99**, 115 (1921); Z. Elektrochem. **22**, 11 (1916).
- (15) GOLDSCHMIDT, H., AND UDDEBY, O.: Z. physik. Chem. **60**, 728 (1907).

- (16) LINDERSTRÖM-LANG, K.: Dansk. Tids. Farm. **2**, 201 (1928).
- (17) MICHAELIS, L., AND MIZUTANI, M.: Z. physik. Chem. **116**, 135 (1925).
- (18) PFEIFFER, P.: Ber. **39**, 1864 (1906); **40**, 4040 (1907).
- (19) SÖRENSEN, S. P. L.: Compt. rend. trav. lab. Carlsberg **8**, 1 (1909); Biochem. Z. **21**, 131 (1909).
- (20) WERNER, A.: Ber. **40**, 4133 (1907). Neuere Anschauungen auf dem Gebiete der anorganischen Chemie, 2nd edition, p. 218. Vieweg, Braunschweig (1909).

HETEROCYCLIC NITROGEN COMPOUNDS

EDWARD C. FRANKLIN AND FRANCIS W. BERGSTROM

Department of Chemistry, Stanford University, California

PART I. PENTACYCLIC COMPOUNDS¹

EDWARD C. FRANKLIN

Received March 9, 1935

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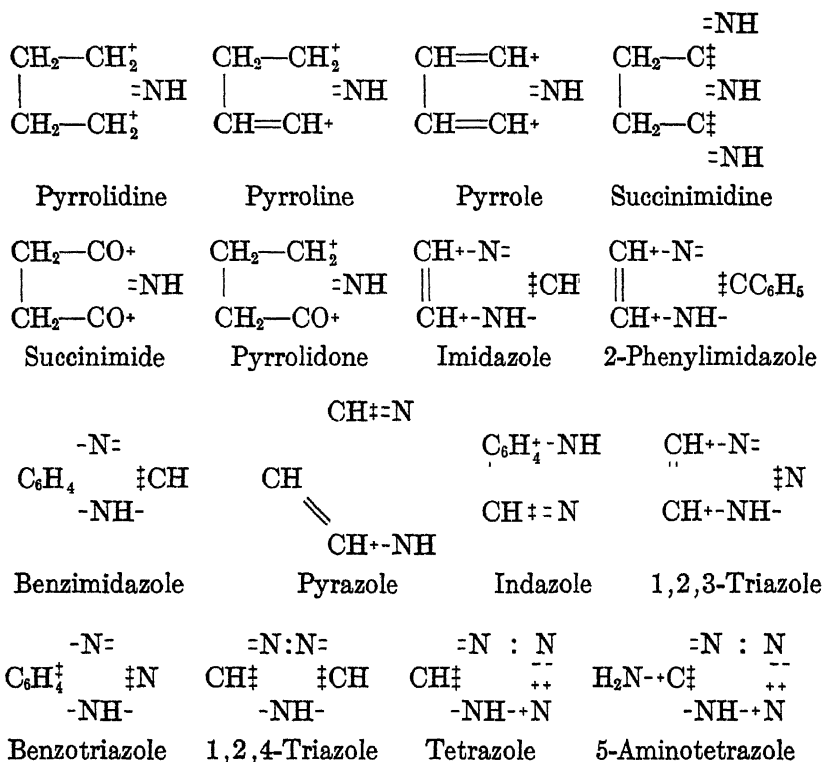
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¹ Part II is to appear in a later issue.

I. INTRODUCTION

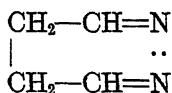
In the first part of this paper the attempt is made to contribute something to our knowledge of the structure of the pentacyclic compounds containing one, two, three, and four nitrogen atoms in the ring. In the second part hexacyclic compounds containing nitrogen will be discussed. It will be shown that all these compounds may be regarded as belonging to the nitrogen system of compounds (41).

Making use of the formulas, RCH_2^+ , RCH^+ , RC^+ , and ^+C , to indicate the augmentation state of carbon as it may be assumed to exist in the primary alcohols, the aldehydes, the carbylic acids, and the carbonic acids—thereby ignoring the carbon to carbon and the carbon to hydrogen polarities—and the symbols, $N\equiv$, $=N:N=$, $-N::N-$, and $N^{\ddagger}$, to represent nitrogen as it may be assumed to be present in ammonia, hydrazine, the azo compounds, and the nitrous acids respectively (41), we venture to write the following formulas.²



² The small plus and minus signs are used to represent covalent bonds which are more or less polar. They do not indicate ionization. For example, in the formulas, $C_2H_5-Na^+$ (106b), CH_2^+-H , $CH_3:CH_3$, CH_3^+-Cl , $CH_3^+-NH_2$, CH_3^+-OH , and CH_3^+-F ,

which respectively represent pyrrolidine as a saturated ammono alcohol, pyrroline and pyrrole as unsaturated ammono alcohols, succinimidine as an ammonosuccinic acid, succinimide as an aquo-ammonosuccinic acid, pyrrolidone³ as a carboxazylic acid ester, imidazole as an ammonoformic acid ester of an unsaturated diatomic alcohol, 2-phenylimidazole as an ammonobenzoic acid ester, benzimidazole as *o*-phenylene ammonoformate, pyrazole as a tautomeric form of a malondialdehyde hydrazone,



indazole as a compound which is at the same time a phenylenehydrazine and an aldehyde hydrazone, 1,2,3-triazole as an ammononitrous acid ester, benzotriazole as *o*-phenylene ammononitrite, 1,2,4-triazole as a diformic acid hydrazide, tetrazole as a formic acid nitrous acid hydrazide, and 5-aminotetrazole as a carbonic acid nitrous acid hydrazide.

Since all covalent links between unlike atoms are more or less polar (71), it is reasonable enough to write the above formulas in which the carbon atoms are represented as positive in respect to the nitrogen atoms. However one can hardly say baldly that one of the nitrogen atoms in 1,2,3-triazole, for example, is positive to the other two, or that 5-aminotetrazole contains residues of nitrous acid and hydrazine, as represented by the

the polarities indicated by the plus and minus signs vary all the way from sodium ethyl, in which the ethyl group is a negative ion, to methyl fluoride in which the methyl group is highly positive (71, 84a). The colons and double colons are used to represent non-polar bonds or unions concerning the polarity of which no assumptions are made.

Excepting that we shall consistently make use of the symbols $=\text{N}:\text{N}=\text{}$ and $-\text{N}::\text{N}-$ for keeping track of hydrazine and azo nitrogen we shall for the most part write formulas after the familiar practice of the organic chemist, making use of plus and minus signs only when it is deemed that clarity will thereby be enhanced. The word "augmentation" will be used from time to time to mean oxidation in the broad general sense (41). The term "carbylic acid" has been adopted as a group name to include the carboxylic acids, the carboxazylic acids or acid amides, and the car-bazylic acids or acid amidines. Because of the trivalency of nitrogen, strict nitrogen analogs of the aquo aldehydes are impossible. The aldehyde-imines, $\text{RCH}=\text{NH}$, which are aldehydes and at the same time either alcohols or acids, we have chosen to call aldehyde-alcohols. Schiff bases, $\text{RCH}=\text{NR}$, we shall call aldehyde-ethers; compounds of the formulas, $\text{RCH}=\text{N}(\text{RCO})$ and $\text{RCH}=\text{N}(\text{RCNH})$, aldehyde-esters. We have taken the liberty of expanding the designation "acetal" to include hydrobenzamide, $(\text{C}_6\text{H}_5\text{CH}=\text{N})_2\text{CHC}_6\text{H}_5$, and similar compounds such as trioxymethylene and paraldehyde. Hydrobenzamide we choose to call a dialdehydeacetal, paraldehyde a cyclic acetal (32, 41).

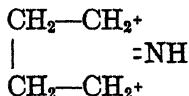
³ The cyclic carbazylic acid ester in which the oxygen present in pyrrolidone is replaced by an imide group is unknown. In order to keep this paper within reasonable limits we shall only now and then mention cyclic compounds containing oxygen.

formulas given above. None the less we shall find as we proceed that, in so far as conclusions concerning the constitution of such cyclic compounds may be drawn from their methods of preparation, the formulas given receive a definite justification. Moreover we shall find that methods for opening many of these remarkably stable rings are known which lend support to the assumption that the nature of the compounds listed is, in a reasonable enough sense, represented by the respective formulas. One may perhaps say that the groups indicated are potentially present or that they are present in somewhat the same sense that ethylene unions are present in benzene. The formulas may be said to represent resonance phases of the respective compounds.

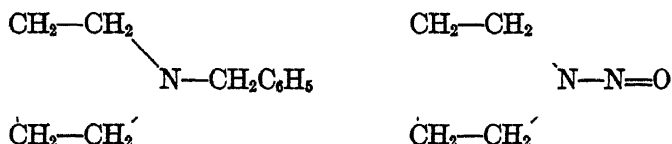
II. COMPOUNDS CONTAINING ONE NITROGEN ATOM IN THE RING

Three pentacyclic compounds containing one nitrogen atom in the ring are pyrrolidine, pyrroline, and pyrrole. These compounds are so obviously amines, or in other words ammono alcohols, as to make it unnecessary to discuss them in any considerable detail here.

A. Pyrrolidine

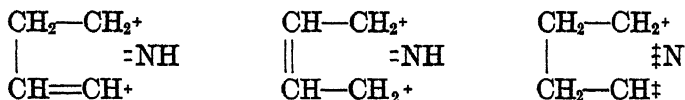


This formula represents a saturated cyclic primary ammono alcohol of which *N*-benzylpyrrolidine and *N*-nitrosopyrrolidine

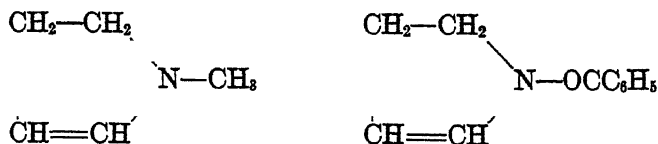


are respectively an ether and an aquo-ammononitrous acid ester.

B. Pyrroline

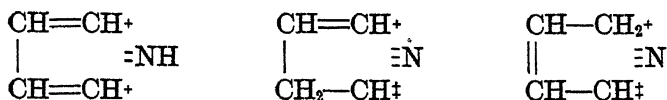


Of these tautomeric formulas the first two represent pyrroline as a cyclic unsaturated ammono alcohol. The third represents a cyclic aldehyde-ether. *N*-Methylpyrroline and *N*-benzoylpyrroline



are respectively a pyrroline methyl ether and a pyrroline aquo-ammonobenzoate.

C. Pyrrole



This compound is usually represented by the first formula without the plus and minus signs. It is, however, very probably a tautomeric compound and as such may be looked upon either as an unsaturated cyclic ammono alcohol (the first formula), or as an unsaturated cyclic aldehyde-ether as represented by the second and third formulas.

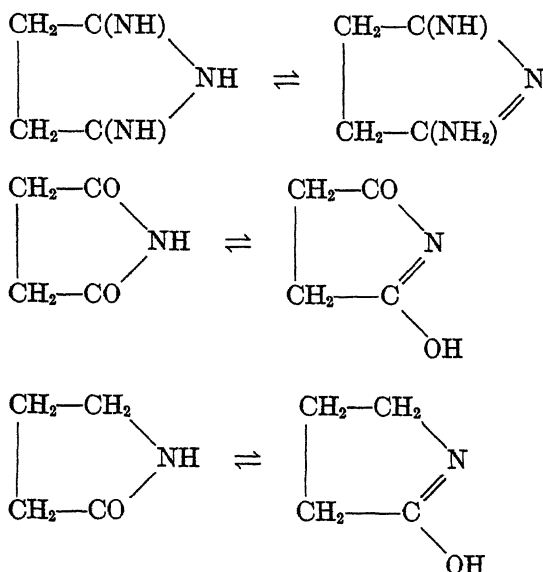
N-Alkylpyrroles are ammono ethers. *N*-Ethylpyrrole, for example, which has been prepared by the action of ethyl iodide on potassium pyrrole, remains unchanged under the action of potassium hydroxide and is decomposed by aqueous hydrochloric acid only at high temperatures. *N*-Acetylpyrrole, which is an acetic acid ester of pyrrole, has been obtained by the interaction of pyrrole and acetic anhydride and by the action of acetyl chloride on pyrrole potassium. As an ester acetylpyrrole is readily hydrolyzed by the action of potassium hydroxide solution to yield pyrrole and potassium acetate.

The first formula above, which represents pyrrole as an unsaturated ammono alcohol or, in other words, as a deammonation product of the tautomeric form of the succindialdehyde-alcohol represented by the formula, $\text{H}_2\text{N—CH=CH—CH=CH—NH}_2$, contains an imino group as a member of a ring in which two ethylene unions are present. In view of the negative influence of these double bonds it might well be expected that pyrrole would show properties distinctly more acid than do the saturated ammono alcohols. The following metallic salts of pyrrole have been obtained by means of reactions carried out in liquid ammonia solutions (40): sodium pyrrole, $\text{C}_4\text{H}_4\text{NNa}$, and $\text{C}_4\text{H}_4\text{NNa}\cdot\text{NH}_3$; calcium pyrrole, $(\text{C}_4\text{H}_4\text{N})_2\text{Ca}$, and $(\text{C}_4\text{H}_4\text{N})_2\text{Ca}\cdot 4\text{NH}_3$; magnesium pyrrole, $(\text{C}_4\text{H}_4\text{N})_2\text{Mg}\cdot 2\text{NH}_3$; and silver pyrrole, $\text{C}_4\text{H}_4\text{NAg}\cdot\text{NH}_3$. In a similar manner potassium indole, $\text{C}_8\text{H}_6\text{NK}$, sodium indole, $\text{C}_8\text{H}_6\text{NNa}$, calcium indole, $(\text{C}_8\text{H}_6\text{N})_2\text{Ca}\cdot 4\text{NH}_3$, magnesium indole, $(\text{C}_8\text{H}_6\text{N})_2\text{Mg}\cdot 4\text{NH}_3$, silver indole, $\text{C}_8\text{H}_6\text{NAg}\cdot\text{NH}_3$, potassium carbazole, $\text{C}_{12}\text{H}_8\text{NK}$, $\text{C}_{12}\text{H}_8\text{N}\cdot\text{NH}_3$, and $\text{C}_{12}\text{H}_8\text{NK}\cdot 3\text{NH}_3$, silver carbazole, $\text{C}_{12}\text{H}_8\text{NAg}\cdot\text{NH}_3$ and $\text{C}_{12}\text{H}_8\text{NAg}\cdot 2\text{NH}_3$,

and calcium carbazole $(C_{12}H_8N)_2Ca \cdot 4NH_3$ and $(C_{12}H_8N)_2Ca \cdot 7NH_3$, have been prepared (40).

D. Succinimidine, succinimide, and pyrrolidone

These compounds may be represented by the following respective pairs of tautomeric formulas

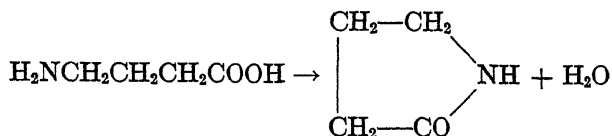


Concerning succinimidine and succinimide it will suffice present purposes to note that they are respectively an ammonosuccinic acid and an aquo-ammonosuccinic acid.

Some considerations which support the view that pyrrolidone is a cyclic carboxazylic acid ester are the following.

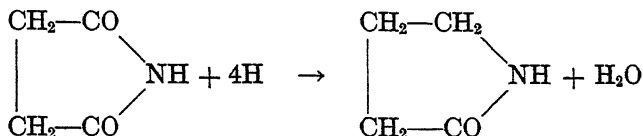
(1) It is formed by heating γ -aminobutyric acid and inversely is hydrolyzed to this aminocarboxylic acid under the action of alkalis or mineral acids (43).

The equation

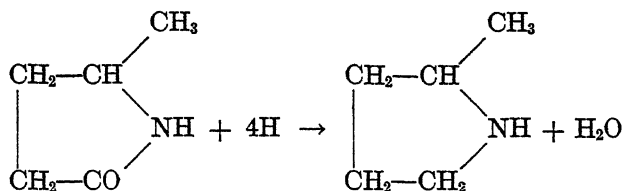


represents the intramolecular esterification of a compound which is at the same time an ammono alcohol and a carboxylic acid to form a cyclic carboxazylic acid ester. The inverse reaction consists in the hydrolysis of the cyclic ester to the open chain alcohol-acid.

(2) Pyrrolidone is formed also by the electrolytic reduction of succinimide (95), the action involved consisting in the conversion of a cyclic acid to a cyclic ester acid as represented by the equation



(3) While pyrrolidone apparently has not been reduced to pyrrolidine it does happen that 2-methylpyrrolidone has been reduced to 2-methylpyrrolidine (94, 14), as represented by the equation



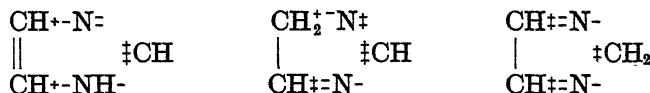
in accordance with which a cyclic carboxazylic acid ester is reduced to a cyclic ammono alcohol.

(4) Since pyrrolidone is formally an acid ester it should be capable of forming metallic salts. Accordingly a sodium salt, $\text{C}_4\text{H}_5\text{ONNa}$, is obtained as a crystalline precipitate when sodium hydroxide is added to a concentrated solution of pyrrolidone in alcohol or water (96). A hydrated mercuric salt, $(\text{C}_4\text{H}_5\text{ON})_2\text{Hg} \cdot \text{H}_2\text{O}$, which loses its water of crystallization at 100°C ., has also been prepared. Moreover pyrrolidone vigorously attacks the alkali metals with evolution of hydrogen.

III. COMPOUNDS CONTAINING TWO NITROGEN ATOMS IN THE RING

The known pentacyclic compounds containing two nitrogen atoms in the ring are imidazole and pyrazole, together with their derivatives.

A. Imidazole

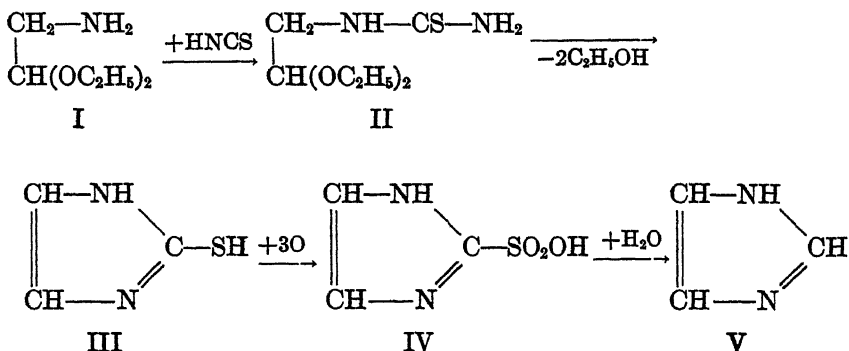


The first formula, which is the generally accepted one, represents imidazole as an ammonoformic acid ester of either the one or the other of the unsaturated alcohols, $\text{HOCH}=\text{CHOH}^4$ or $\text{H}_2\text{NCH}=\text{CHNH}_2$; the

⁴ This compound is unknown excepting in so far as it may exist in tautomeric equilibrium with glycol aldehyde. The nitrogen analog is quite unknown.

second represents it as a compound which is a formic acid ester in respect to the upper union of the formic acid group and a formic acid acetal of glycol aldehyde in respect to the lower. The third formula may be said to represent a cyclic acetal containing glyoxal and formaldehyde residues.

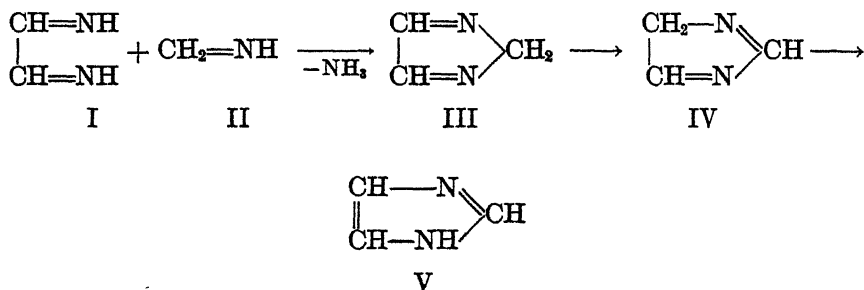
1. *Formation.* (a) Carrying out a series of reactions summarized by the scheme



Marekwald (67) prepared imidazole and concluded that its constitution must be represented by formula V.

When the hydrochloride of the aminoacetaldehyde-acetal (I) is treated with potassium thiocyanate the thiourea derivative (II), which was not analyzed, is formed. On heating this compound at 140°C. intramolecular ammonolysis takes place, forming ethyl alcohol and compound III, which Marekwald named imidazolylmercaptan. This ethylenyl thioammonocarbonate, when warmed in solution in 10 per cent nitric acid, yields imidazole (V) and sulfuric acid, presumably by way of the unknown sulfonic acid (IV).

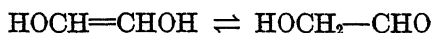
(b) Assuming that imidazole is a cyclic ammonoformate its formation by the interaction of glyoxal, formaldehyde, and ammonia (78) may be represented by the scheme



in accordance with which the dialdehyde-diimine (I) and the formaldehyde-imine (II) formed, it may be surmised, by the action of ammonia on glyoxal and on formaldehyde, respectively, react with each other with the elimination of ammonia to form III. This hypothetical formaldehyde glyoxal acetal, undergoing an intramolecular Cannizzaro reaction, passes over into the formic acid ester acetal (IV) which, by intramolecular rearrangement identical in principle with the keto-enol transformation, is converted into imidazole (V).

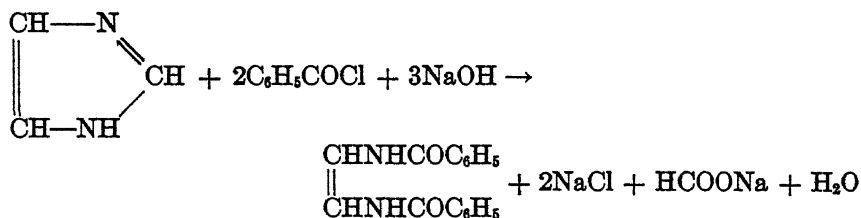
Of course the simplest interpretation of this method for the preparation of imidazole is to the effect that it is a cyclic acetal (formula III above).

2. *Opening the ring.* Assuming imidazole established as a cyclic ethylenyl ammonoformate, one might expect to find it hydrolyzable to aquoformic acid, ammonia, and perhaps glycolaldehyde



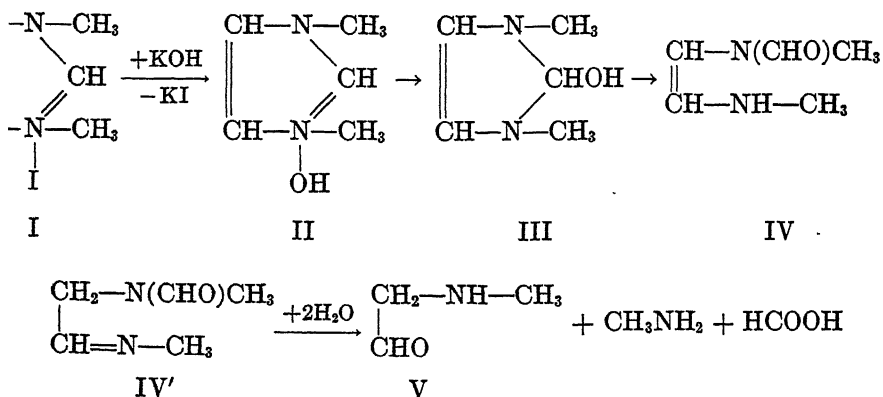
As a matter of fact, imidazole resists the action of acids and alkalis. However, several methods are known whereby the opening of the imidazole ring has been effected.

(a) When imidazole is treated with benzoyl chloride and sodium hydroxide (Schotten-Baumann reagent), even at temperatures as low as 0°C ., dibenzoyldiaminoethylene and sodium formate are formed quantitatively (6).



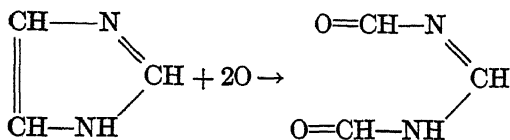
The reactions as thus represented consist in the conversion of a cyclic formic acid ester into an open chain aquo-ammonobenzoate of an unsaturated diatomic alcohol and sodium aquoformate. In principle an ammonoformic acid ester is hydrolyzed to an ammono alcohol and aquoformic acid.

(b) When the quaternary ammonium salt, I below, formed by the action of methyl iodide on 1-methylimidazole, is boiled with strong potassium hydroxide solution, good yields of methylamine and formic acid are obtained (82, 76). The successive reactions involved may be represented by the scheme

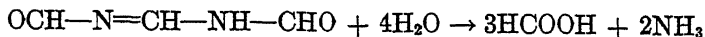


and explained as follows. The quaternary ammonium hydroxide (II), formed by the action of potassium hydroxide on the iodide (I), rearranges to compound III in a manner resembling, in essence, the decomposition of tetramethylammonium hydroxide to form trimethylamine and methyl alcohol. Compound III is an ester of an aquo-ammonooorthoformic acid, $\text{HC}(\text{NH}_2)_2\text{OH}$. Such a compound, being an acid ester, should be unstable and therefore ready to pass over into the open chain compound IV. In the presence of potassium hydroxide solution the tautomeric form (IV') of this compound, which is at the same time an aldehyde-ether (lower branch) and a formic acid ester (upper branch), should undergo hydrolysis to form methylamine, formic acid, and perhaps the unknown methylamino-acetaldehyde (V). The appearance of formic acid and methylamine among the reaction products supports the view that 1-methylimidazole is a cyclic ammonoformate. No one of the compounds represented by the formulas II, III, IV, IV', and V was isolated.

3. *Oxidation.* Reducing agents are without action on imidazole. Wyss (108) identified carbon dioxide and formic acid as products of the action of potassium permanganate on imidazole. The formation of formic acid may be explained on the assumption that a cyclic formate is oxidized at the ethylene union, as represented by the equation



and that the unknown triformic acid thus formed undergoes hydrolysis to yield aquoformic acid and ammonia



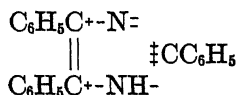
Wyss, however, does not mention ammonia as one of the reaction products (cf. p. 318).

Radzisewski (79) found oxamide among the products formed by the action of hydrogen peroxide on imidazole. His observation is readily interpreted as supporting any one of the formulas given above.

4. *Metallic salts.* Since imidazole is an acid ester it should be capable of forming metallic salts. A silver salt, obtained as an amorphous precipitate by adding silver nitrate to a water solution of imidazole, has long been known. Using liquid ammonia as solvent in which to carry out the necessary reactions Wenzel (102) prepared the imidazole salts listed herewith: $C_3H_3N_2Na \cdot NH_3$, $C_3H_3N_2K \cdot NH_3$, $(C_3H_3N_2)_2Mg \cdot 4NH_3$, $(C_3H_3N_2)_2Mg \cdot NH_3$, $(C_3H_3N_2)_2Ca \cdot 2.5NH_3$, $(C_3H_3N_2)_2Ca \cdot 1.5NH_3$, $C_3H_3N_2Ag$. The zinc and cobalt salts, $(C_3H_3N_2)_2Zn$ and $(C_3H_3N_2)_2Co$, have been prepared by the action of imidazole on salts of the respective metals in aqua ammonia solution (30).

Clearly the methods of preparation of imidazole and the reactions it undergoes lend support to the view that it is a cyclic ammonoformate.

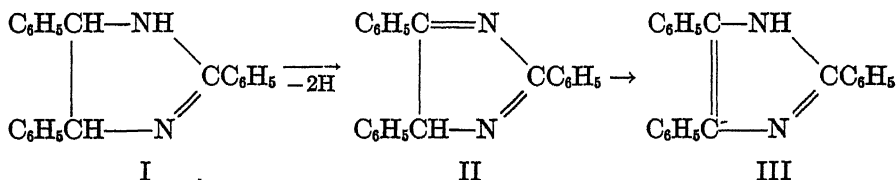
B. Lophine, 2,4,5-triphenylimidazole



Just as the preceding discussion has shown that imidazole may be regarded as a cyclic ammonoformic acid ester, so in harmony with the view that lophine is a cyclic ammonobenzoic acid ester are the methods for its preparation and the numerous reactions which it has been observed to undergo.

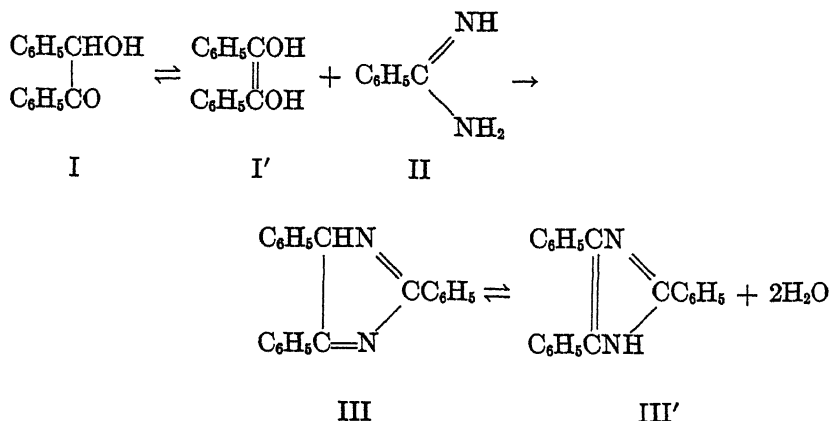
1. *Formation.* (a) By the action of oxidizing agents in water solution (38) and of iodine in liquid ammonia solution amarine, which is a dihydride of lophine, is converted into lophine. Also simply by heating amarine, or allowing it to stand in liquid ammonia solution in the presence of potassium amide, lophine is formed (92).

Making use of Japp and Moir's formulas for amarine and lophine (58), the augmentation of any one of the stereoisomeric forms of amarine to lophine may be represented by the scheme



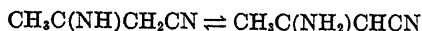
The first step involves the augmentation (dehydrogenation) of one of the secondary alcohol groups present in amarine (I) to a ketone group in formula II; the second consists in an intramolecular rearrangement which is strictly analogous to the familiar keto-enol transformation.⁵ It is of course possible that I is dehydrogenated directly to III, in which case a saturated carbon to carbon union is augmented to an ethylene union.

(b) In agreement with our assumption that lophine is a cyclic ammonobenzoate is its formation by the action of benzamidine (an ammonobenzoic acid) on benzoin (61) in accordance with the equation



Assuming that the constitution of lophine is as represented by formula III', one may say either that the tautomer (III), formed by the interaction of benzamidine (II) and benzoin (I), undergoing a keto-enol transformation is converted into lophine (III'), or that the tautomeric form of benzoin (I') reacts with benzamidine to give lophine directly. Formula III'

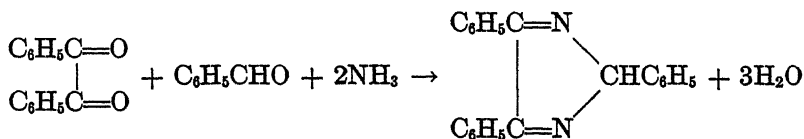
⁵ Just as the keto-enol rearrangement takes place in accordance with the reversible equation, $\text{RCOCHR}_2 \rightleftharpoons \text{RC(OH)CR}_2$, so it is reasonable to expect analogous compounds belonging to the nitrogen system ready to undergo similar rearrangements. Diacetonitrile, for example, behaves under certain conditions in accordance with the first, under others with the second of the formulas,



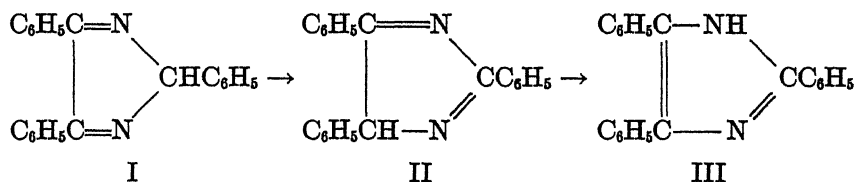
Indeed, as it seems, this compound has been established as existing in two isomeric forms as represented by the preceding formulas (69). Perhaps the most extensively investigated tautomeric compound known to exist in both the keto and enol forms is acetoacetic ester. The nitrogen analog of acetoacetic acid would be β -iminobutyramidine, $\text{CH}_3\text{C(NH)CH}_2\text{C(NH)NH}_2$, which is unknown. However diacetonitrile, $\text{CH}_3\text{C(NH)CH}_2\text{CN}$, which is the anammonide of β -iminobutyramidine, is formed from acetonitrile under much the same conditions as acetoacetic ester is formed by the aldol condensation of ethyl acetate, and in many respects resembles acetoacetic ester in its behavior.

represents lophine as a cyclic ammonobenzoate of an unsaturated diatomic alcohol. As represented by the formula III, it is at the same time a ketone benzoic acid acetal and an ammonobenzoic acid ester.

(c) Radzisevski (78) prepared lophine by heating equimolecular quantities of benzil and benzaldehyde with alcoholic or aqueous ammonia. As represented by the equation

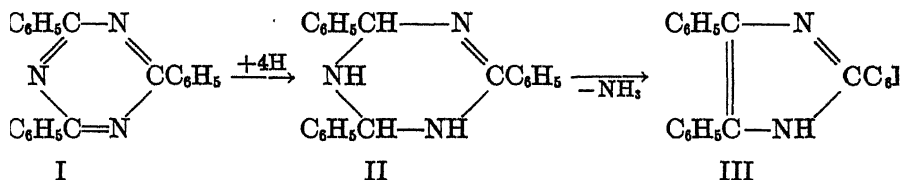


this method of preparation would seem to imply that lophine is a benzaldehyde diketone-acetal. Since, however, lophine is fairly certainly established (58) as a cyclic benzoate, it is to be concluded that the above-formulated product of the interaction of benzil, benzaldehyde, and ammonia undergoes rearrangement in accordance with the scheme,



which represents the intramolecular augmentation of the benzaldehyde group in I to the benzoic acid group in II, and the concomitant reduction of the one of the ketone groups to a secondary alcohol group and finally the enolization of II to III.

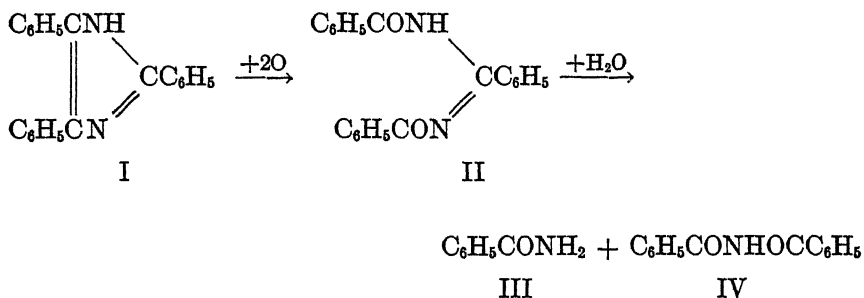
(d) Lophine has been obtained by the reduction of cyaphenine (77), the reactions involved probably taking place as represented by the scheme



in accordance with which two of the benzoic acid groups in the trimeric benzoic anammonide (I) undergo reduction to benzaldehyde groups in II, following which this dibenzaldehyde benzoic acid acetal loses ammonia to form lophine (III).

2. *Oxidation.* Lophine is very resistant to the action of reducing agents. Apparently it has not been reduced to amarine, from which it is formed by

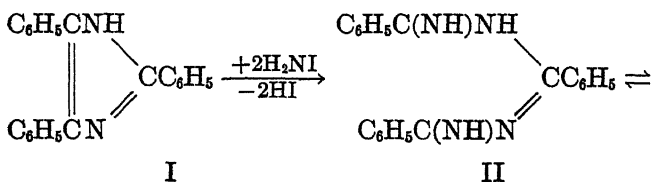
oxidation (11, 57) and by nitridation (p. 315). On the other hand it is readily attacked by oxidizing agents. On warming with chromic acid in dilute acetic acid solution lophine is quantitatively oxidized to benzamide and dibenzamide (38, 59) in a manner which may be represented by the scheme

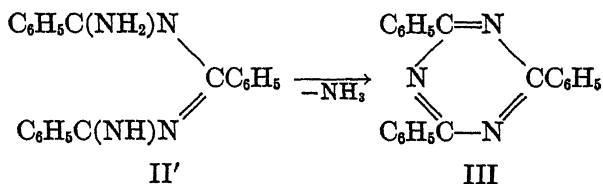


It is assumed that oxidation at the double bond converts lophine into an unknown tribenzoic acid (II), which in turn is hydrolyzed to equimolecular quantities of the two aquo-ammonobenzoic acids III and IV. The imidazole ring in lophine is opened just as in imidazole itself under the action of potassium permanganate.

In aqueous alkaline solution lophine is converted into aquobenzoic acid and ammonia by the action of atmospheric oxygen (77). Here again it is fair to say that lophine is oxidized to dibenzoylbenzamidine, formula II above, which in the presence of strong alkali is hydrolyzed completely to aquobenzoic acid and ammonia.

3. *Nitridation.* If we are justified in our assumption that the primary product of the action of oxidizing agents on lophine is the tribenzoic acid represented by the formula II above, then it is reasonable to expect that nitridation agents will attack lophine in a similar manner to form the ammonotribenzoic acid, formula II below, which hypothetical compound may either take up ammonia to form benzamidine or lose ammonia to give benzonitrile or its trimer. As a matter of fact, by the nitridizing action of iodine in liquid ammonia solution lophine is converted into cyaphenine (91) as represented, let us say, by the scheme

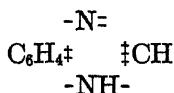




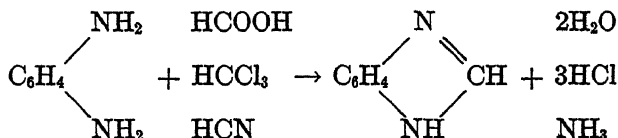
4. *Metallic salts.* Since lophine contains an ammonobenzoic acid hydrogen atom,⁶ it is an acid ester and should in consequence thereof be capable of forming metallic salts.

Using liquid ammonia as solvent in which to effect the necessary reactions Strain (91) has prepared the salts listed herewith: $\text{C}_{21}\text{H}_{15}\text{N}_2\text{K}$, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{K} \cdot 3\text{NH}_3$, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Na}$, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Li}$, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Li} \cdot x\text{NH}_3$, $(\text{C}_{21}\text{H}_{15}\text{N}_2)_2\text{Ca}$, $(\text{C}_{21}\text{H}_{15}\text{N}_2)_2\text{Ca} \cdot 6\text{NH}_3$, $(\text{C}_{21}\text{H}_{15}\text{N}_2)_2\text{Mg} \cdot 2\text{NH}_3$, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Ag}$, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Ag} \cdot 2\text{NH}_3$, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Cu}$, $(\text{C}_{21}\text{H}_{15}\text{N}_2)_2\text{Cu}$, and $(\text{C}_{21}\text{H}_{15}\text{N}_2)_2\text{Cu} \cdot x\text{NH}_3$. The potassium, sodium, and lithium salts were obtained by the action of lophine on the respective metallic amides; the calcium salt by the action of lophine on calcium amide and on metallic calcium; the magnesium salt by the action of lophine on metallic magnesium; the silver salt by the action of lophine on silver amide and also by the action of potassium lophine on silver nitrate; the cuprous salt by the action of lophine on ammonous cuprous nitride, $\text{Cu}_3\text{N} \cdot x\text{NH}_3$; the cupric salt by bringing together solutions of potassium lophine and cupric nitrate. Most of these salts were obtained well crystallized and of sharply definite composition. They are all hydrolyzed by the action of water to lophine and the respective metallic hydroxides or oxides.

C. Benzimidazole



Three reactions whereby this bicyclic compound has been prepared (107, 46, 22) may be summarized by means of the scheme

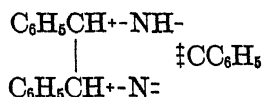


⁶ This hydrogen atom may of course be looked upon as alcoholic hydrogen as well as acid hydrogen. Since, however, the acid group contributes much more to the mobility of the hydrogen atom than does the alcohol group, it is reasonable in this and other similar cases to speak of acid hydrogen.

which is a formic acid ester, and its hydrolysis, presumably by way of V, to *N,N'*-dimethyl-*o*-phenylenediamine (VI) and aquoformic acid supports the view that benzimidazole is a cyclic *o*-phenylene ammonioformate. Compound IV was also obtained by Fischer and Fussenegger (33) by heating *N,N'*-dimethylphenylenediamine with excess of formic acid.

Using liquid ammonia as solvent in which to carry out the reactions involved, the following formulated salts have been obtained (106a): $C_7H_5N_2Na$, $C_7H_5N_2Li \cdot 2NH_3$, $C_7H_5N_2Li$, $(C_7H_5N_2)_2Ba \cdot NH_3$, $(C_7H_5N_2)_2Ba$. Other salts of benzimidazole which have been prepared are $C_7H_5N_2Ag$, $(C_7H_5N_2)_2Cu$, $(C_7H_5N_2)_2Cd$, $(C_7H_5N_2)_2Co$, and $(C_7H_5N_2)_2Zn$. A mercury salt of the formula, $C_7H_5N_2HgCl$, is known (8, 30), as are also alkyl and acyl derivatives such as $C_7H_5N_2CH_3$ and $C_7H_5N_2OCC_6H_5$.

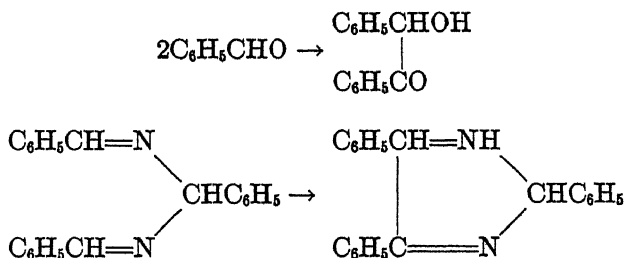
D. Amarine, 2,4,5-triphenyl-4,5-dihydroimidazole



This formula, which has been established by Japp and Moir (51), represents amarine as a cyclic hydrobenzoin ammonobenzoate.

1. *Formation.* (a) It has long been known that hydrobenzamide, when heated alone or with potassium hydroxide solution, is converted into an isomer known as amarine. More recently it has been found by Strain (91) that the same rearrangement takes place when hydrobenzamide is warmed in liquid ammonia solution with potassium amide.

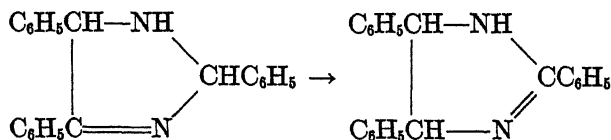
Since hydrobenzamide is a near analog of benzaldehyde it would be reasonable to expect it to undergo a benzoin condensation, just as benzaldehyde is known to condense to benzoin. The respective reactions involved may be represented by the equations



In the first case with the establishment of a carbon to carbon union, two molecules of benzaldehyde are converted into a mixed ketone secondary alcohol. In the second, the same carbon to carbon union is established and at the same time a hydrogen atom from one of the aldehyde groups

wanders to the nitrogen atom of the other, thereby converting the one aldehyde group into a secondary alcohol group and the other into a ketone group.

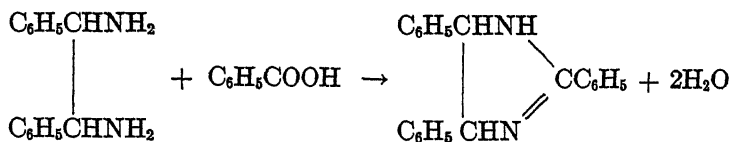
However, as has been shown by Japp and Moir, amarine has the constitution represented by the second formula herewith.



It follows therefore that the transformation of the assumed primary condensation product of hydrobenzamide into amarine involves an intramolecular Cannizzaro reaction, which is to say that the benzaldehyde group at the right-hand end of the first formula is augmented to a benzoic acid group as shown in the second, while concomitantly the ketone group is reduced to a secondary alcohol group.

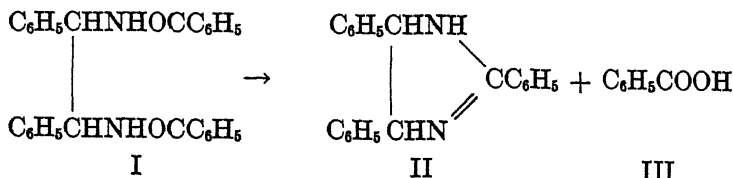
(b) Radziszewski (78) prepared amarine by the interaction of benzoin, benzaldehyde, and ammonia, and concluded that it should be represented by the first of the formulas above. Since, however, the second formula has been established (58) as representing amarine we must conclude that Radziszewski's assumed product undergoes intramolecular augmentation and reduction to form amarine.

(c) Japp and Moir (58) have shown that isoamarine is formed as represented by the equation



when the racemic form of diphenylethylenediamine is heated with aquobenzoic acid. The aquobenzoic acid acts on a diatomic ammono alcohol to form a cyclic ammonobenzoate.

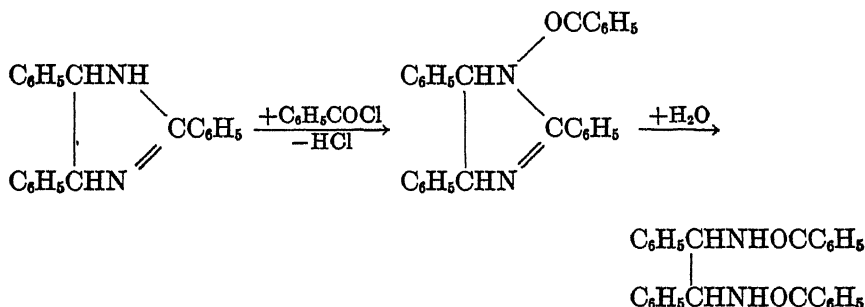
(d) Isoamarine has also been obtained by heating the racemic form of dibenzoyldiphenylethylenediamine, formula I below, in a current of hydrochloric acid gas (31, 58). The reaction involved, which is represented by the equation



consists in the conversion of an open chain aquo-ammonobenzoate into a cyclic ammonobenzoate and aquobenzoic acid. By an intramolecular process one of the aquo-ammonobenzoic acid groups in I is ammonolyzed to an ammonobenzoic acid group in II, the other being simultaneously hydrolyzed to aquobenzoic acid. The reaction involved is similar to that which takes place when acetamide is converted into equimolecular quantities of acetic acid and acetamidine under the action of hot dry hydrochloric acid.

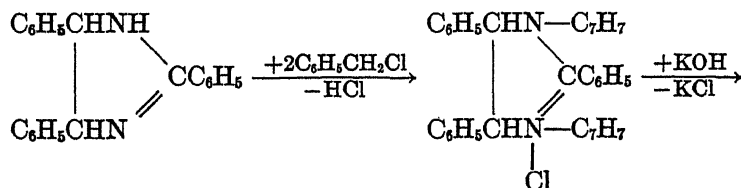
2. *Opening the dihydromidazole ring.* Although amarine has not been hydrolyzed to diphenylethylenediamine and aquobenzoic acid, or to hydrobenzoin, aquobenzoic acid, and ammonia, as might perhaps be expected on the assumption that it is a benzoic acid ester of diphenylethylenediamine, it does happen that procedures for opening the amarine ring are known which are to be regarded as accomplishing such a hydrolytic decomposition.

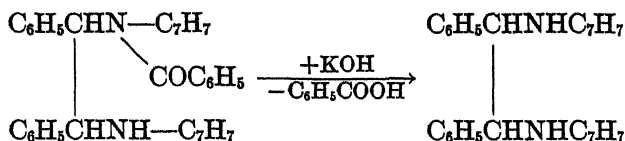
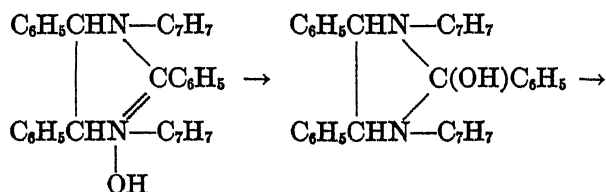
(a) When treated with a benzene solution of benzoyl chloride amarine yields benzoylamarine which in turn, under the action of alcoholic hydrochloric acid, is converted into dibenzoyldiphenylethylenediamine (58). As represented by the scheme (cf. p. 313),



a cyclic benzoate is first and last converted into an open chain aquo-ammonobenzoate. The first and second formulas represent cyclic benzoates; the last an open chain benzoate.

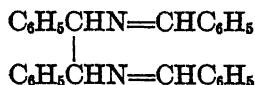
(b) Japp and Moir (58) converted amarine into symmetrical dibenzoyldiphenylethylenediamine (last formula below) and aquobenzoic acid by means of a series of reactions represented by the scheme (cf. p. 320).





Compounds represented by the third and fourth formulas were not isolated. The amarine ring is opened to form an open chain derivative of diphenylethylenediamine, which is a diatomic ammono alcohol, and aquobenzoic acid. In principle amarine may be said to undergo hydrolytic decomposition.

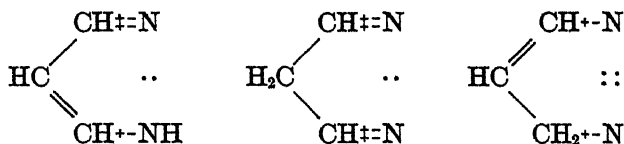
3. *Oxidation and reduction.* The augmentation of amarine to lophine has already been discussed (p. 315). By the action of metallic sodium on amarine small yields (20 per cent) of a compound represented by the formula



have been obtained (48, 58, 36). Whatever the mechanism of the reactions involved may be, which is not obvious, the net result, in so far as the formation of the above-formulated compound is concerned, consists in the reduction of an ammonobenzoic acid ester to a dibenzaldehyde-ether.

4. *Metallic salts.* Silver salts of both amarine and isoamarine, $\text{C}_{21}\text{H}_{17}\text{N}_2\text{Ag}$, are known (86, 19). A sodium salt of isoamarine has been isolated, though its composition has not been fixed by analysis (58).

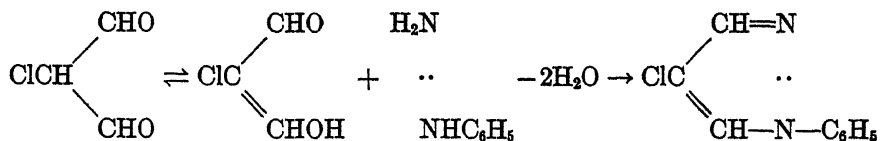
E. Pyrazole



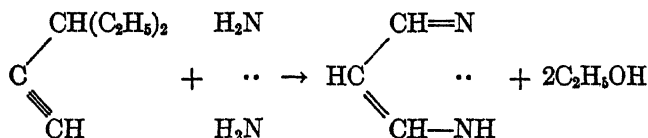
The first two formulas represent tautomeric forms of a cyclic malondialdehyde hydrazone; the third represents a cyclic azo compound. In the first formula one of the hydrazine nitrogen atoms is attached to aldehyde

carbon, in the other to alcohol carbon. In the second formula both hydrazine nitrogen atoms are in combination with aldehyde residues. The first formula is the generally accepted one.

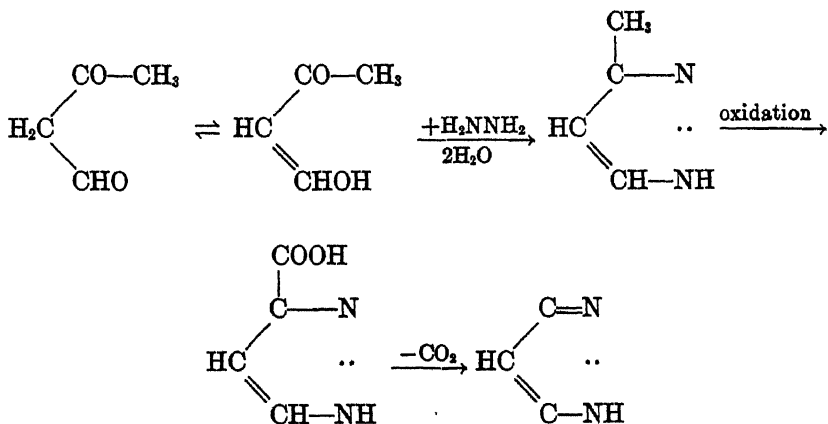
1. *Formation.* Regarding pyrazole as a cyclic malondialdehyde hydrazone, it would be reasonable to expect that it might be prepared by the interaction of malondialdehyde, a somewhat indefinitely known compound, and hydrazine. Now while such a reaction is unknown it does happen that 1-phenyl-4-chloropyrazole has been obtained by the action of phenylhydrazine on chloromalondialdehyde in alcohol solution (23) as represented by the equation



and that pyrazole itself has been prepared by the action of hydrazine on propargyldiethylacetal (18).

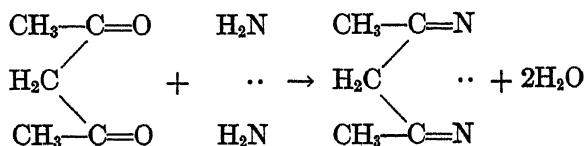


Starting with acetoacetic aldehyde (18a) pyrazole has furthermore been made as represented by the scheme



A quantitative yield of 3,5-dimethylpyrazole appears when acetylacetone, hydrazine sulfate, and sodium hydroxide are brought together in

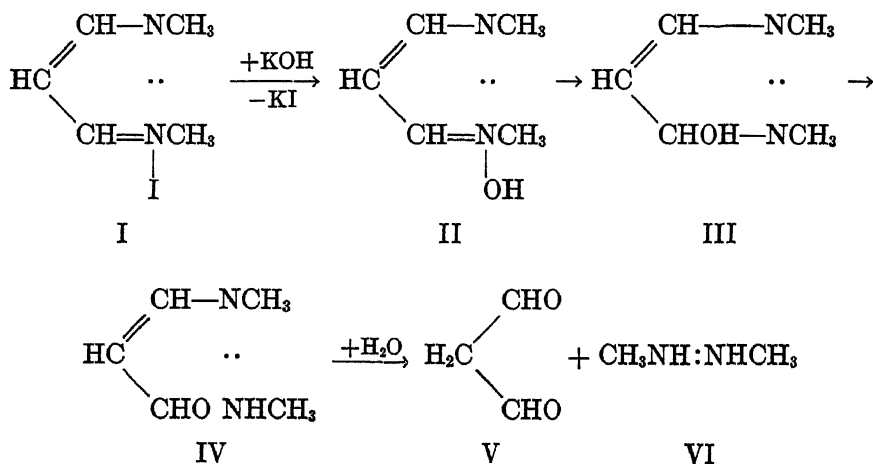
water solution (81). The reactions here involved take place in accordance with the equation



which represents the action of hydrazine on a diketone to form a cyclic diketone hydrazone.

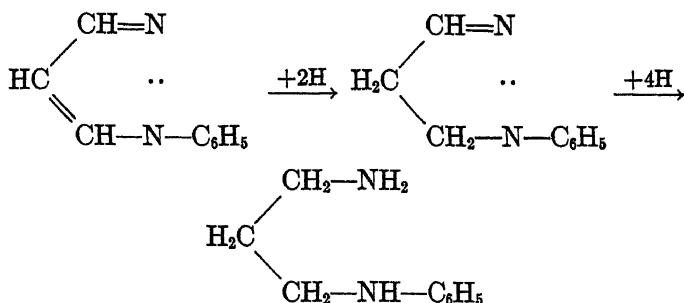
2. *Opening the ring.* Pyrazole is a very stable compound. It is aromatic in character and shows but few of the properties of open chain derivatives of hydrazine. Nevertheless under certain conditions the hydrazine group, which we assume to be present (or potentially present) in the pyrazole ring, reveals itself, as the following discussion will show.

(a) The quaternary salt, I below, which is formed by the action of methyl iodide on 1-methylpyrazole, yields all of its nitrogen in the form of symmetrical dimethylhydrazine when heated with strong potassium hydroxide solution (59, 60). Symmetrical dimethylhydrazine is formed by the hydrolysis of the quaternary salt in accordance, let us say, with the scheme:



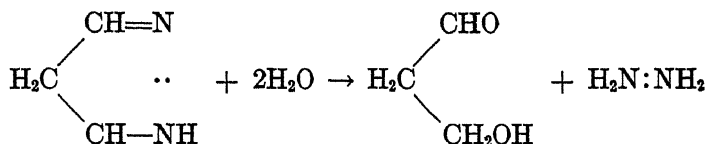
Formula III contains an aldehyde hydrazone hydrate group, $\text{RCH}(\text{OH})\text{-NR:NR}_2$, which makes for the ready rearrangement of a compound of this formula into the open chain compound IV. It is assumed that by the action of aqueous potassium hydroxide on IV, symmetrical dimethylhydrazine and presumably malondialdehyde (V) are formed. None of the compounds represented by the formulas II, III, IV, and V was identified. Considerable amounts of formic acid were present in the reaction mixture.

(b) Pyrazole resists the action of reducing agents. However 1-phenylpyrazole has been reduced first to 1-phenylpyrazoline and thence to 1-amino-3-phenylaminopropane (3, 4) as represented by the scheme



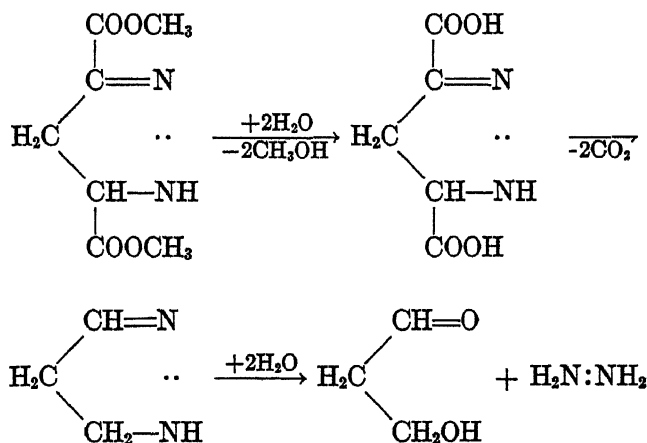
In so far as the opening of the ring is concerned, the action involved consists in the reduction of hydrazine nitrogen to ammonia nitrogen.

(c) A fair yield of hydrazine is obtained when pyrazoline is heated with concentrated hydrochloric acid, the reaction involved probably taking place as represented by the equation



though hydracrylaldehyde was not identified (21).

(d) The dimethyl ester of pyrazoline-3,5-dicarboxylic acid (first formula below) gives abundant yields of hydrazine when heated with dilute sulfuric acid (16). The reactions involved may be represented by the scheme



though the products formed other than carbon dioxide and hydrazine remain unknown.

3. *Metallic salts.* A sodium salt, which was not analyzed, a silver salt, $C_3H_3N_2Ag$, and a pyrazole mercuric chloride, $C_3H_3N_2HgCl$, have been prepared (15). Rosengarten (80) prepared a silver salt, $C_6H_7N_2Ag \cdot H_2O$, and a mercuric salt, which was not analyzed, of 2,5-dimethylpyrazole. It may be noted that, formally, neither pyrazole nor dimethylpyrazole is an ammono acid. It seems fair however to say that the hydrazine hydrogen atom becomes distinctly more acid under the negative influence of the pyrazole ring. It will be recalled that alkali metal derivatives of hydrazine are known.

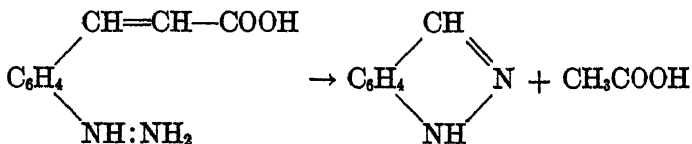
F. Indazole



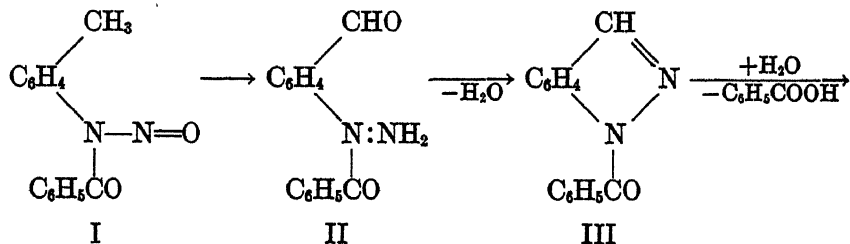
The first formula represents indazole as a cyclic hydrazinobenzaldehyde hydrazone, the second as a cyclic azo compound.

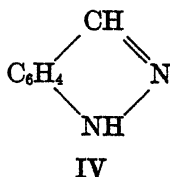
1. *Formation.* Methods for the preparation of indazole and 3-methylindazole, which are in agreement with the assumption that they are derivatives of hydrazine, are the following.

(a) Simply by heating hydrazinocinnamic acid indazole is formed (35), the reaction involved taking place as represented by the equation



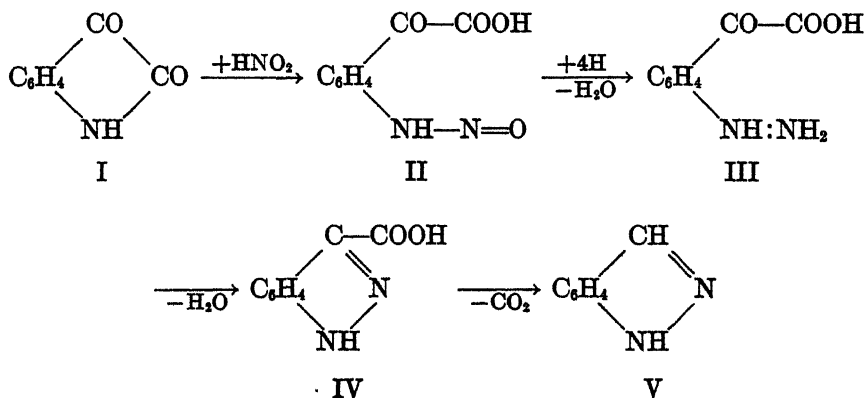
(b) Indazole is formed in good yield when benzoyl-*o*-tolynitrosamine, formula I below, which is a benzoyltolyl derivative of an aquo-ammononitrous acid, is warmed in contact with dry benzene (56). The reactions involved may be represented by the scheme





which is to say that by an intramolecular reaction the methyl group in I is augmented to an aldehyde group in II, while at the same time the nitrous acid group is reduced to the hydrazine group. The unknown benzoylhydrazinobenzaldehyde (II) thus formed loses water to yield the likewise unknown benzoylindazole (III). It may be assumed that the water formed in the conversion of II into III hydrolyzes the latter to indazole (IV) and benzoic acid.

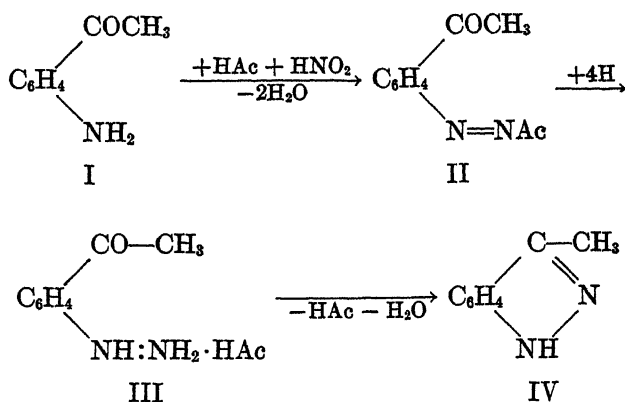
(c) When *o*-diazophenylglyoxylic acid, formula II below, formed by diazotizing isatin (I) in dilute sulfuric acid solution, is reduced by the action of sulfur dioxide and stannous chloride, the *o*-hydrazinophenylglyoxylic acid (III), which is formed, loses water and passes over into the indazolecarboxylic acid (IV). Simply by heating this compound somewhat above its melting point a quantitative yield of indazole is obtained (84). The successive steps may be represented by the scheme



By the action of the reducing agent the nitrous acid group present in II is converted into the hydrazine group in III which, it is fair to assume, persists as such in the final product (V).

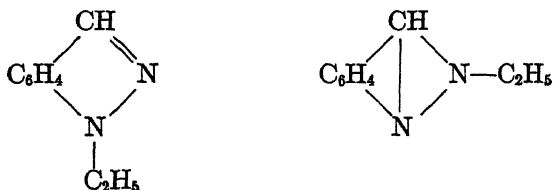
Imidazole is not known to enter into reactions which support the view that it contains a hydrazine residue.

(d) 3-Methylindazole (IV) has been prepared from *o*-aminoacetophenone (34, 3, 4) by way of the diazo and hydrazine derivatives II and III as represented, in effect, by the scheme



Under the action of nitrous acid the amino compound (I) is converted into the diazo compound (II), which latter compound on reduction yields III. With the elimination of water and acid this hydrazine derivative passes over into 3-methylindazole (IV).

2. *N-Alkylindazoles*. Two *N*-ethylindazoles have been prepared, to which the formulas



have been given (1a, 2). The first formula may reasonably be said to represent a derivative of hydrazine. The second formula we must perforce let stand without comment other than to note that in a highly speculative way one may write the formulas

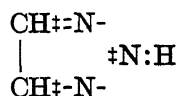
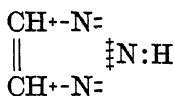
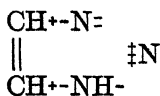


and say that they represent derivatives of hydrazine.

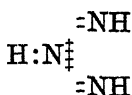
3. *Metallic salts*. Fischer and Tafel (37) prepared a silver and a mercury salt of indazole, which were later shown (56) to have the composition represented by the respective formulas $\text{C}_7\text{H}_5\text{N}_2\text{Ag}$ and $(\text{C}_7\text{H}_5\text{N}_2)_2\text{Hg}$.

IV. COMPOUNDS CONTAINING THREE NITROGEN ATOMS IN THE RING

Compounds containing three nitrogen atoms in a pentacyclic ring are 1,2,3-triazole and 1,2,4-triazole, and their derivatives.

A. 1, 2, 3-Triazole⁷

The first formula represents an ethylenyl ester of the one tautomeric form of ammononitrous acid, $\text{HN}=\text{N}^+-\text{NH}_2$, the second an ester of the other form,

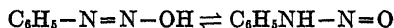


Indulging in a little wishful thinking it is perhaps not altogether unreasonable to say that the third formula represents a cyclic glyoxal hyponitrous acid acetal.⁸

Some of the methods for the preparation of 1,2,3-triazole and its derivatives are readily interpreted as supporting the view that they are derivatives of an ammononitrous acid; others, while not forbidding such a view, are perhaps better explained as resulting in the formation of compounds

⁷ A colon is printed between the nitrogen and hydrogen atoms in the second and third formulas, as well as in others to follow, as a convenient means of indicating that no assumptions are made concerning the polarity of these unions. The NH group in the first formula represents an ammonia residue in which of course the nitrogen atom is negative in respect to the hydrogen atom. For a reasonable justification of the symbol representing pentapositive nitrogen as given in the second formula, see Franklin, *The Nitrogen System of Compounds*, p. 44 (reference 41).

⁸ Franklin (41) has shown that Stieglitz' suggestion to the effect that the diazo compounds are derivatives of nitrous acid (93) is supported by a wealth of observations. Diazobenzene, in so far as it may be represented by the formulas,



is a phenyl ester of an aquo-ammononitrous acid, $\text{HN}=\text{N}-\text{OH} \rightleftharpoons \text{H}_2\text{N}-\text{N}=\text{O}$. If we accept Angeli's formula, $\text{C}_6\text{H}_5\text{N}(\text{NH})\text{O}$, diazobenzene may even be looked upon as a phenyl derivative of the tautomeric form of aquo-ammononitrous acid represented by the formula, $\text{H}:\text{N}(\text{NH})\text{O}$, or in other words it may be said to be nitrobenzene in which one of the oxygen atoms is replaced by an imido group.

Since nitrous acid is generally assumed to be a tautomeric compound to which the formulas $\text{HO}-\text{N}=\text{O}$ and $\text{H}:\text{N}\text{O}_2$ may be given, one may speculate to the effect that aquo-ammononitrous acid, known in liquid ammonia solution (83), exists in the tautomeric forms represented by the formulas,

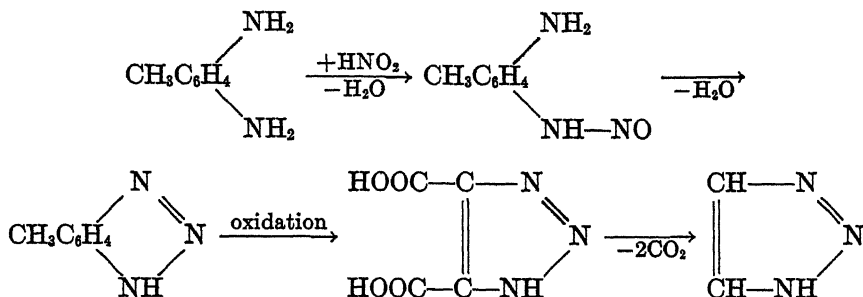


and that to the ammononitrous acid, known only in the form of esters, the formulas, $\text{H}_2\text{N}-\text{N}=\text{NH} \rightleftharpoons \text{H}:\text{N}(\text{NH})_2$, may be given. For the reason that they are not available in this type face these above formulas are perforce printed without the small plus and minus signs.

containing nitrogen atoms linked together by non-polar bonds. So also certain of the reactions which 1,2,3-triazole and its derivatives undergo are in agreement with the assumption that they contain an ammonitrous acid group; others that they are rather derivatives of an unknown triazene, $\text{HN}::\text{N}:\text{NH}_2$.

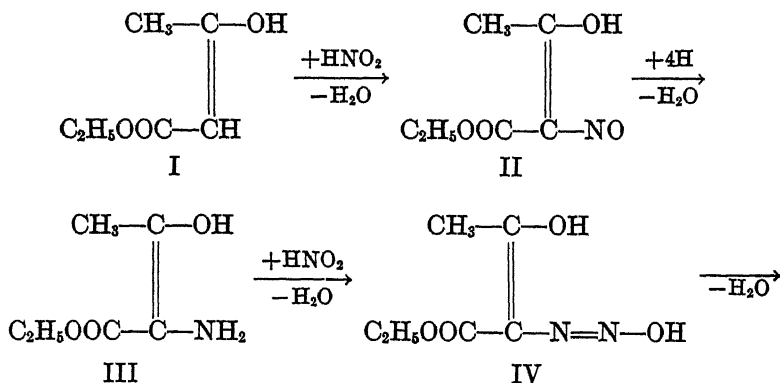
1. *Formation.* The following described methods for the preparation of 1,2,3-triazole and some of its derivatives lend support to the assumption that they are, at least potentially, so to say, cyclic ammonitrites.

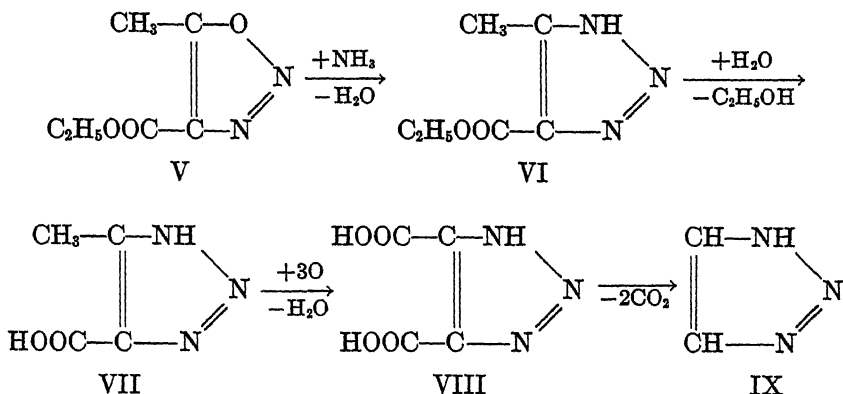
(a) Ladenburg (62) found that a toluotriazole, third formula below, is formed by the interaction of potassium nitrite and 3,4-diaminotoluene sulfate. When this cyclic ammonitrite is warmed with alkaline potassium permanganate solution it is oxidized to a triazoledicarboxylic acid, which, on heating somewhat above its melting point, yields carbon dioxide and 1,2,3-triazole (13). The reactions involved are represented by the scheme



It is interesting to note that the triazole ring, which we assume to contain a nitrous acid residue, is more resistant to the action of oxidizing agents than is the benzene ring.

(b) Starting with acetoacetic ester good yields of 1,2,3-triazole have been obtained (103) by means of reactions summarized by the scheme





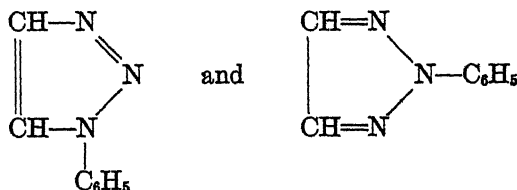
By the action of nitrous acid on acetoacetic ester (I) the nitroso compound (II) is formed, which on reduction gives III. It is assumed that this aminoacetoacetic acid ester, under the action of nitrous acid, is converted into the diazo compound (IV). This unknown compound loses water to form the cyclic aquo-ammononitrite (V), which is ammonolyzed to the triazole derivative (VI) by the action of ammoniacal ammonium acetate solution. Compound VI on hydrolysis yields the carboxylic acid (VII), which has been oxidized to VIII. Bladin (13) observed the decomposition of this dicarboxylic acid to form 1,2,3-triazole (IX) and carbon dioxide.

(c) The formation of 1,2,3-triazole by the interaction of acetylene and hydrazoic acid (27) may be explained as involving the augmentation of acetylene to an ethylene derivative, and the concomitant reduction either of nitric acid nitrogen to nitrous acid nitrogen or of hydrazine nitrogen to ammonia nitrogen as represented by the equations

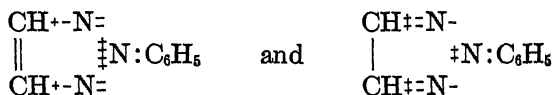


B. Phenyl-1,2,3-triazoles

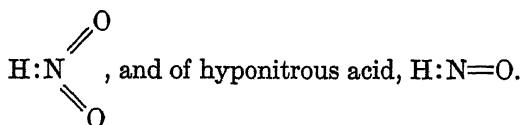
Two phenyl-1,2,3-triazoles have been prepared, to which the respective formulas



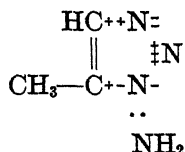
have been given (24, 72a). The first formula may clearly be said to represent a cyclic ethylenyl phenyl ammononitrite. For the second isomer, named *N*-phenylosotriazole by von Pechmann (72a), the formulas



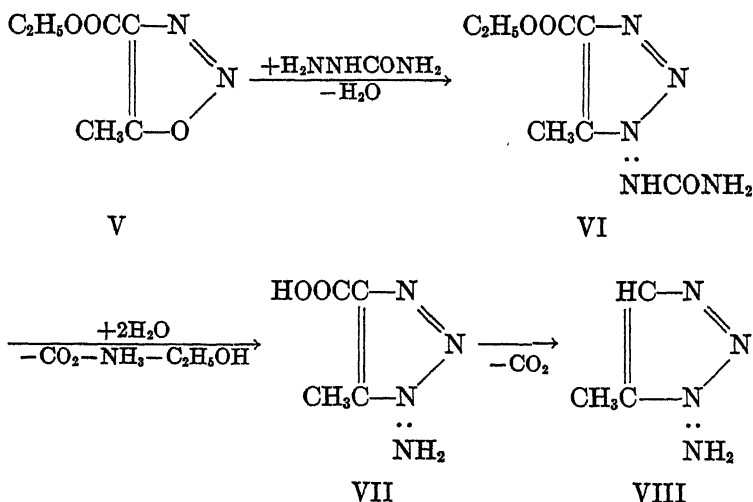
may be written and in a highly speculative way be said to represent derivatives of nitrobenzene and nitrosobenzene, respectively; which is to say that they are derivatives of the tautomeric form of nitrous acid,



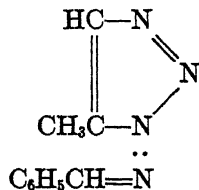
C. 1-Amino-3-methyl-1,2,3-triazole



1-Amino-1,2,3-triazole is not known. However, starting with the anhydride of diazoacetic acid ester, formula V (p. 333 and below), Wolff and Hall (106), following processes represented herewith,

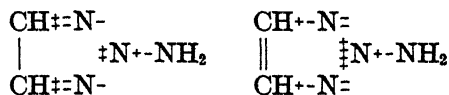


prepared 1-amino-5-methyl-1,2,3-triazole (VIII). The reactions involved may reasonably be said to result in the formation of a cyclic compound which is a derivative of an unknown nitrous acid hydrazide, $H_2N-N=N:NH_2$. The formation of a benzaldehyde hydrazone

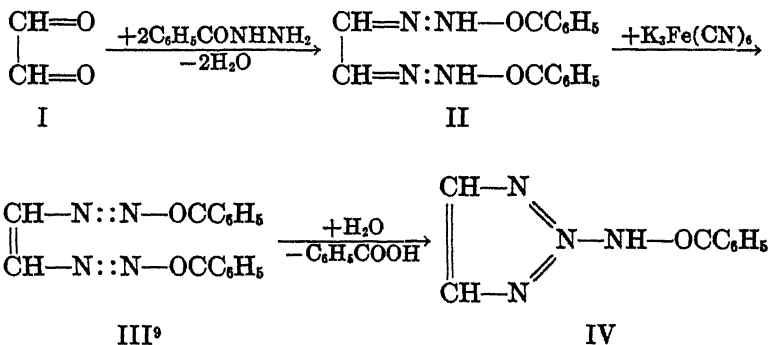


by the action of benzaldehyde on this aminotetrazole supports the view that it contains a hydrazine residue, as represented by formula VIII above.

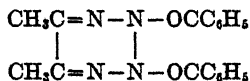
D. 2-Amino-1,2,3-triazole



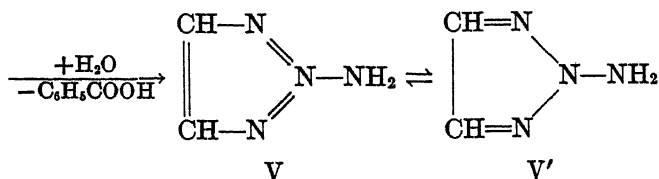
As represented by these formulas this compound, to which von Pechmann gave the name *N*-aminoösotriazole, is either a glyoxal nitrous acid acetal or an ethylenyl ammononitrate. It has been prepared by a sequence of reactions (72, 88, 89), summarized by the scheme



⁹ This compound has not been isolated. However, its dimethyl homolog, to which von Pechmann gave the formula

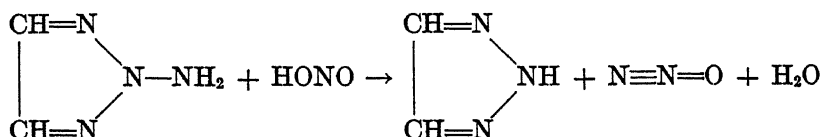


has been prepared (72) by the oxidizing action of potassium ferricyanide on diacetyl-dibenzoyl osazone.

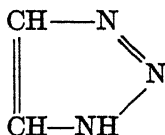


The glyoxal dibenzoylosazone (II), formed by the action of benzoylhydrazine on glyoxal (I), is represented as undergoing oxidation to the azo compound (III). In the presence of warm sodium hydroxide solution this compound yields IV,¹⁰ which on warming with dilute hydrochloric acid is hydrolyzed to V, V', and benzoic acid.

von Pechmann and Bauer (72) found that nitrous acid acts on this *N*-aminoösotriazole to form osotriazole



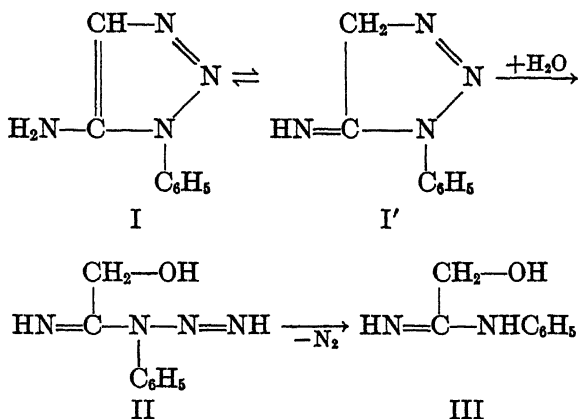
Dimroth (25) later showed that von Pechmann's osotriazole is identical with Bladen's (13) triazole represented by the formula



1. *Opening the ring.* 1,2,3-triazole in comparison with the open chain ammononitrous acid esters, with diazoaminobenzene, for example, is a remarkably stable compound which resists the action of hydrolyzing agents. None the less the ring in a number of 1,2,3-triazole derivatives has been opened by methods which show that such compounds may be regarded as cyclic ammononitrous acid esters. Two procedures whereby the 1,2,3-triazole ring has been opened are as follows.

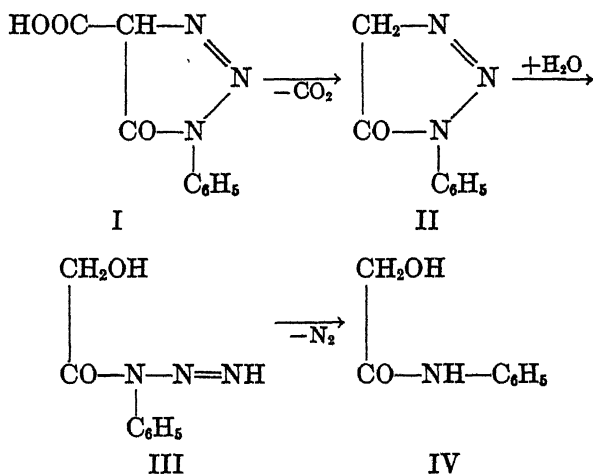
(a) Dimroth (26) found that 1-phenyl-5-amino-1,2,3-triazole (formulas I and I' below) under the action of hot dilute sulfuric acid yields nitrogen and glycolic acid phenylamidine (III below), just as by similar treatment diazoaminobenzene yields nitrogen, phenol, and aniline. It appears in accordance with the scheme

¹⁰ The mechanism of the conversion of III into IV is not clear. It may be said, however, that of the four azo nitrogen atoms contained in III, three are reduced to ammonia nitrogen and the fourth is augmented to nitric acid nitrogen.



that 1-phenyl-5-amino-1,2,3-triazole is first hydrolyzed to the open chain diazo compound (II), and second, that this hypothetical ammonitrous acid derivative loses nitrogen (nitrous anammonide) to form glycolic acid phenylamidine (III).¹¹ This compound was identified by hydrolyzing it to glycolic acid anilide and ammonia. Noting that the group $^+\text{CH}_2\text{C}\ddagger$ characterizes the glycolic acids it may be said that the formulas I, I', and II represent respectively a cyclic and an open chain glycolic acid nitrous acid phenyl ester.

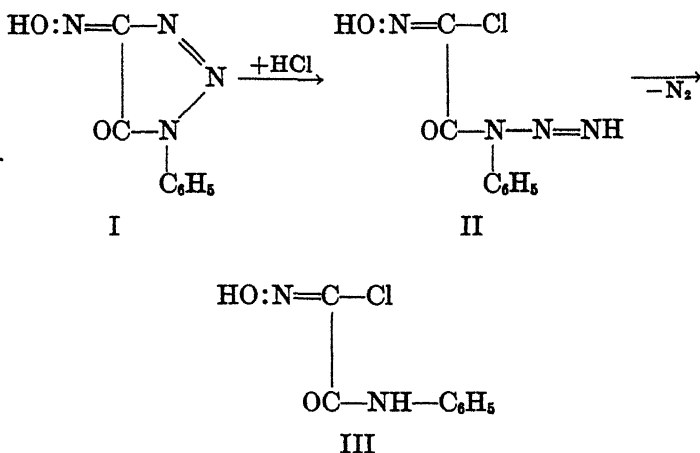
(b) When phenyltriazolonecarboxylic acid (formula I) is heated with water, glyoxylic acid anilide (formula IV), nitrogen, and carbon dioxide are formed (25a) in accordance with the scheme



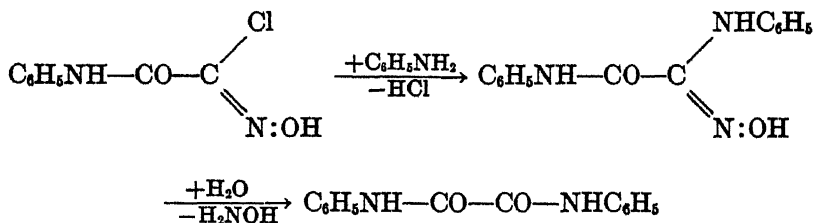
¹¹ Alternately it may be that II is hydrolyzed to III and the very unstable aquo-ammonitrous acid, $\text{HO}-\text{N}=\text{NH}$, which decomposes to form nitrogen and ammonia (83).

in which formulas II and III represent hypothetical compounds. It is assumed that the nitrogen results from the decomposition of the ammononitrous acid residue contained in compound III.

(c) A similar opening of the triazole ring takes place when the 1,2,3-triazole derivative known as 1-phenyl-4-isonitroso-5-triazolone (formula I below) is treated with fuming hydrochloric acid (29). The reactions involved may be represented by the scheme



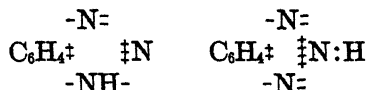
in accordance with which the compound I, which is at the same time an oxalic acid oxime and an ammonooxalic ammononitrous acid phenyl ester, is opened to form II. This hypothetical diazo compound loses nitrogen to form the compound III, which is an oxalic acid oxime-chloride and at the same time an oxalic acid phenyl ester. Dimroth and Traub established the constitution of III by converting it into oxanilide



2. *Metallic salts.* 1,2,3-Triazole shows distinct acid properties just as does diazoaminobenzene. Baltzer and von Pechmann (5) prepared a silver salt, $\text{C}_2\text{H}_2\text{N}_3\text{Ag}$, and a triazole mercuric chloride, $\text{C}_2\text{H}_2\text{N}_3\text{HgCl}$. A blue precipitate, which was assumed to be a cupric salt, was obtained by adding cupric sulfate to a water solution of triazole. Calcium hydroxide

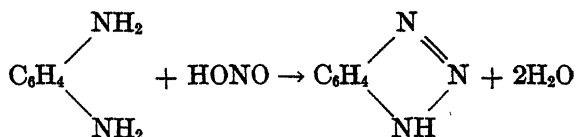
was observed to dissolve in a triazole solution. In ether solution 1,2,3-triazole attacks metallic sodium to form a sodium salt.

E. Benzotriazole

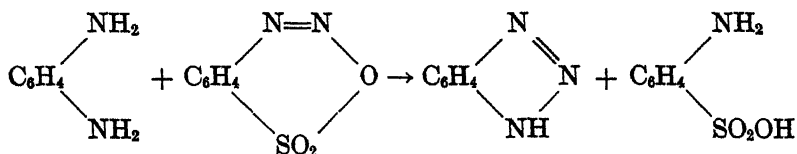


It is reasonable to say that these formulas represent tautomeric forms of *o*-phenylene ammononitrite.

Benzotriazole has been prepared by the action of nitrous acid (62) and of *p*-diazobenzenesulfonic acid (47) on *o*-phenylenediamine. In accordance with the equation



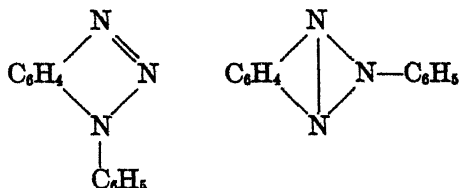
a cyclic *o*-phenylene ammononitrite is formed. As represented by the equation



the same compound is formed by the action of a derivative of aquo-ammononitrous acid on *o*-phenylenediamine.

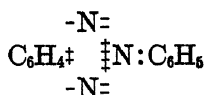
Benzotriazole is a very stable compound which shows none of the reactions of the open chain ammono and aquo-ammononitrous acid esters.

Two phenyl derivatives of benzotriazole are known, to which the respective formulas



have been ascribed (44, 82a, 45). As represented by the first formula, 1-phenylbenzotriazole may obviously be regarded as a cyclic phenyl

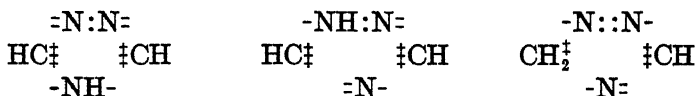
o-phenylene ammononitrite. We venture to give 2-phenylbenzotriazole the formula



which represents it as nitrobenzene in which the two oxygen atoms are replaced by an *o*-phenylenediamine residue (41). In harmony with the assumption that *o*-phenylbenzotriazole is a derivative of nitrobenzene is its ready reduction to *o*-phenylenediamine and aniline (44). However, it must be said in this connection that attempts to prepare 2-phenylbenzotriazole by the interaction of *o*-phenylenediamine and nitrobenzene have not been successful.

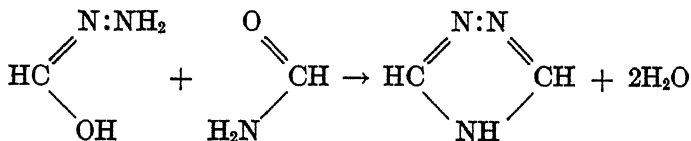
Metallic salts of benzotriazole are apparently unknown. Zincke and Lawson (109) observed the formation of the sodium, $\text{C}_7\text{H}_5\text{N}_3\text{Na}$, silver, $\text{C}_7\text{H}_5\text{N}_3\text{Ag}$, mercury, $(\text{C}_7\text{H}_5\text{N}_3)_2\text{Hg}$, lead, copper, zinc, and cadmium salts of 6-methylbenzotriazole, though the latter four compounds were not analyzed. According to Hofmann (55) 5-nitrobenzotriazole is an acid of sufficient strength to redden sharply a water solution of litmus.

F. 1,2,4-Triazole



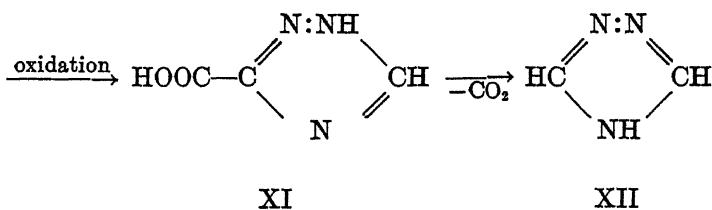
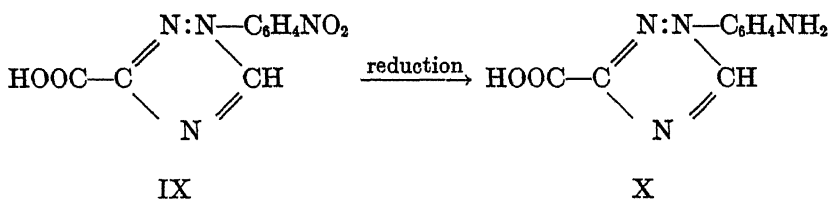
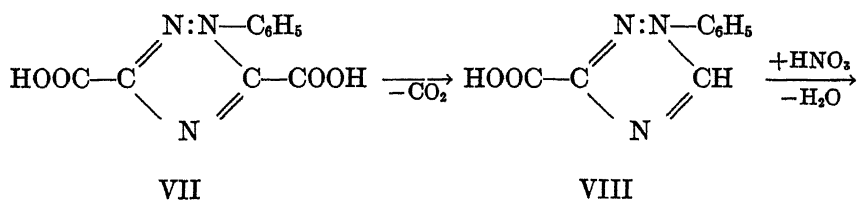
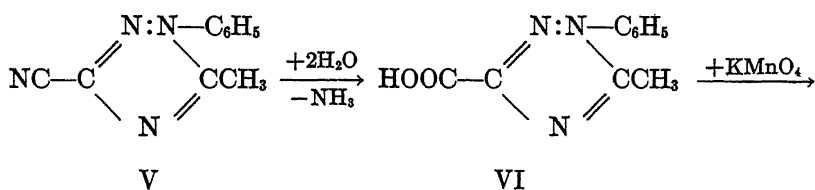
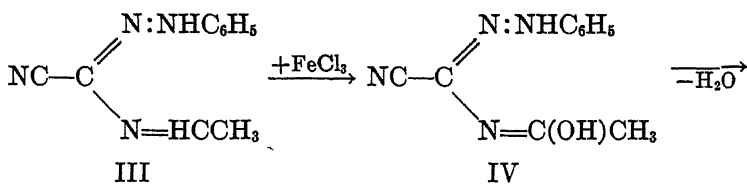
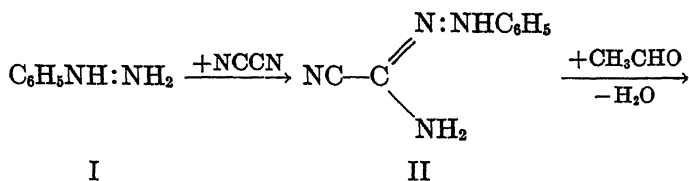
The first two formulas represent assumed tautomeric forms of a cyclic diformic acid hydrazide, the third a cyclic azo compound. The rearrangement of the first and second formulas into the third involves the intramolecular augmentation of hydrazine nitrogen to azo nitrogen and the concomitant reduction of one of the formic acid carbon atoms to formaldehyde carbon.

1. *Formation.* (a) 1,2,4-Triazole is formed by heating a mixture of formylhydrazine and formamide (73, 74). The equation



represents the action of an aquo-ammonoformic acid on a formic acid hydrazide to form a cyclic diformic acid hydrazide.

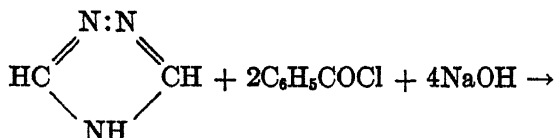
(b) The reactions involved in a second procedure for the preparation of 1,2,4-triazole are summarized by the scheme (11a, 12a, 12b, 12c)



Excepting that the compound represented by formula IV has not been isolated, all the reactions represented are known. Since it appears from the above that the hydrazine residue, $=N:N=$, remains intact in the successive compounds indicated, it is reasonable to conclude from this method of preparation that 1,2,4-triazole is a cyclic diformic acid hydrazide.

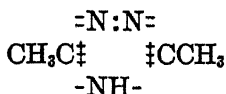
2. *Metallic salts.* Using liquid ammonia as solvent Strain (91) prepared metallic salts of 1,2,4-triazole represented by the following formulas: $C_2H_2N_3Na$, $C_2H_2N_3Ag$, $C_2H_2N_3Ag \cdot NH_3$, $(C_2H_2N_3)_2Mg$, $(C_2H_2N_3)_2Mg \cdot 4NH_3$, $(C_2H_2N_3)_2Ca$, $(C_2H_2N_3)_2Ca \cdot xNH_3$, and $C_2H_2N_3Cu$. The cupric salt, $(C_2H_2N_3)_2Cu$, is also known.

3. *Opening the ring.* 1,2,4-Triazole is a stable compound which, resisting the action of acids and alkalis, has not been hydrolyzed to formic acid, hydrazine, and ammonia as might be expected on the assumption that it is a formic acid hydrazide. However, when 1,2,4-triazole is heated on a water bath with benzoyl chloride and the reaction mass is treated with sodium hydroxide solution, symmetrical dibenzoylhydrazine is obtained in good yield (54). Moreover the reactions involved may be represented by the equation (cf. pp. 313, 320, 323),

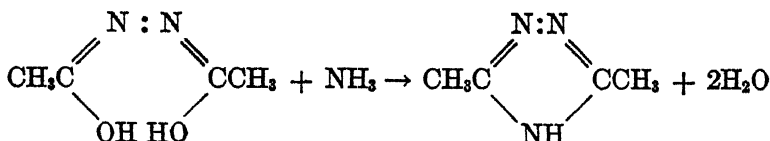


though formic acid and ammonia were not reported among the reaction products.

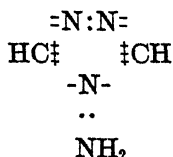
G. *3,5-Dimethyl-1,2,4-triazole*



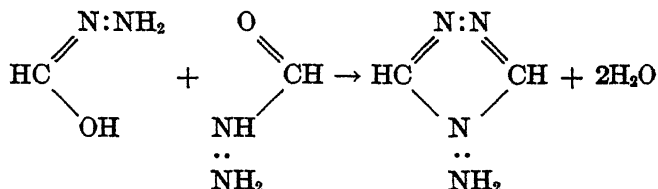
The view that this compound is a cyclic diacetic acid hydrazide is in agreement with its formation in accordance with the equation



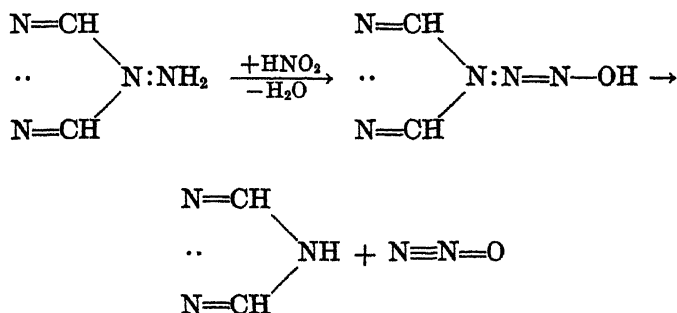
by the ammonolytic action of alcoholic ammonia on diacetylhydrazine at 200°C . (87). A silver salt of this acid hydrazide has been prepared.

H. 4-Amino-1,2,4-triazole

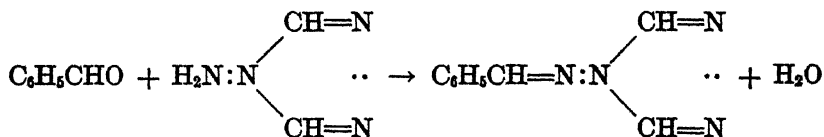
This cyclic formic acid hydrazide has been obtained by heating formylhydrazine at 150°C. (49, 17, 70), the reaction taking place in accordance with the equation



As represented by the above formula, 4-amino-1,2,4-triazole contains two hydrazine residues. The presence of the hydrazine group, which is partly extracyclic, is shown by the conversion of this aminotriazole into 1,2,4-triazole and nitrous oxide by the action of nitrous acid

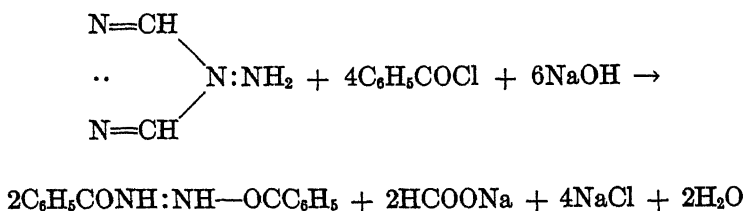


and by its interaction with aldehydes to form hydrazones. Benzaldehyde, for example, acts on 4-amino-1,2,4-triazole as represented by the equation

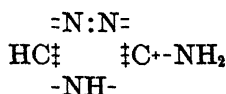


to form a compound which is at the same time a benzaldehyde hydrazone and a formic acid hydrazide (20, 17).

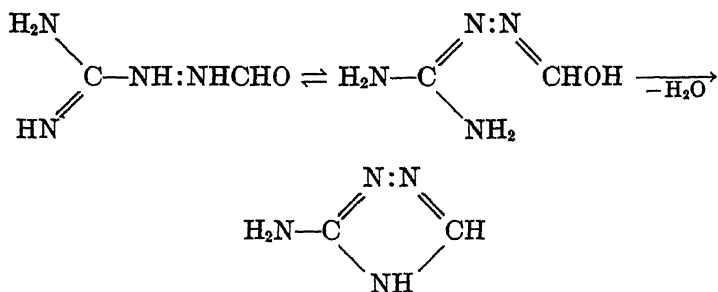
The two hydrazine residues and the two formic acid groups, which we assume to be present in this aminotriazole, are revealed when, under the action of benzoyl chloride and sodium hydroxide (cf. pp. 313, 320, 323, and 342), both hydrazine groups appear as dibenzoylhydrazine and the formic acid residues as sodium formate (49). The reactions involved are represented by the equation



I. 3-Amino-1,2,4-triazole



On treating formylaminoguanidine nitrate¹² with aqueous sodium carbonate it is converted into 3-amino-1,2,4-triazole (98, 100). The reactions involved, which are represented by the scheme

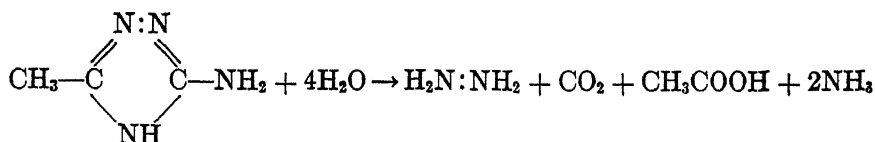


consist in the elimination of water from the open chain carbonic acid formic acid hydrazide thereby converting it into the cyclic hydrazide. Thiele and Manchot (100) had the silver salt of this compound in their hands, but did not analyze it.

Apparently the triazole ring in this cyclic acid hydrazide has not been opened. It happens however that 3-amino-5-methyl-1,2,4-triazole (first

¹² Formylaminoguanidine, first and second formulas below, is a mixed carbonic acid formic acid hydrazide and not in any proper sense an amino compound.

formula below) has been hydrolyzed quantitatively in accordance with the equation,

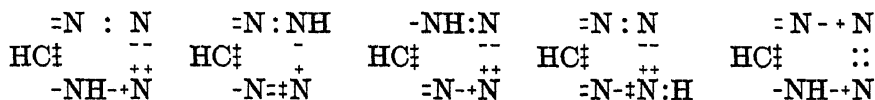


when heated with dilute sulfuric acid at 180°C. (98, 100). This equation may be read as representing the hydrolysis of a cyclic carbonic acid acetic acid hydrazide to hydrazine, carbonic anhydride, aquoacetic acid, and ammonia.

V. COMPOUNDS CONTAINING FOUR NITROGEN ATOMS IN THE RING

The one known pentacyclic ring containing four nitrogen atoms is present in tetrazole and its many derivatives.

A. Tetrazole¹³

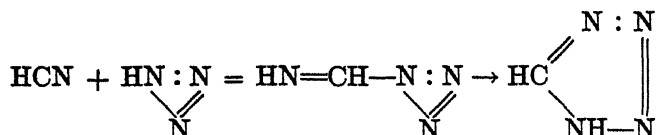


The first four formulas represent hypothetical tautomeric forms of a mixed formic acid nitrous acid hydrazide, the fourth being related to the first as the formula $\text{H:N}(\text{NH})_2$, for an hypothetical ammononitrous acid, is related to the formula $\text{H}_2\text{N-+N}\ddot{\text{N}}\text{=NH}$. It is reasonable to say that these formulas represent tautomeric forms or resonance phases of tetrazole. Certainly no one of them has been established to the exclusion of the others. A fifth possible formula representing tetrazole as a cyclic ammonoformic acid ammonohyponitrous acid is the last one given above.

While the writing of formulas in which one of the nitrogen atoms is represented as ammonia nitrogen, the second as nitrous acid nitrogen, and the remaining two as existing in the state in which nitrogen is present in hydrazine may perhaps appear somewhat naive, we shall nevertheless find that such formulas will be helpful in the following discussion of tetrazole and its derivatives. On the one hand we shall find that the methods of preparing these compounds are in agreement with such formulas. On the other hand, however, it happens that but one of them, namely 5-amino-tetrazole, has been observed to enter into reactions which lend substantial support to our assumptions concerning the nature of the tetrazole ring.

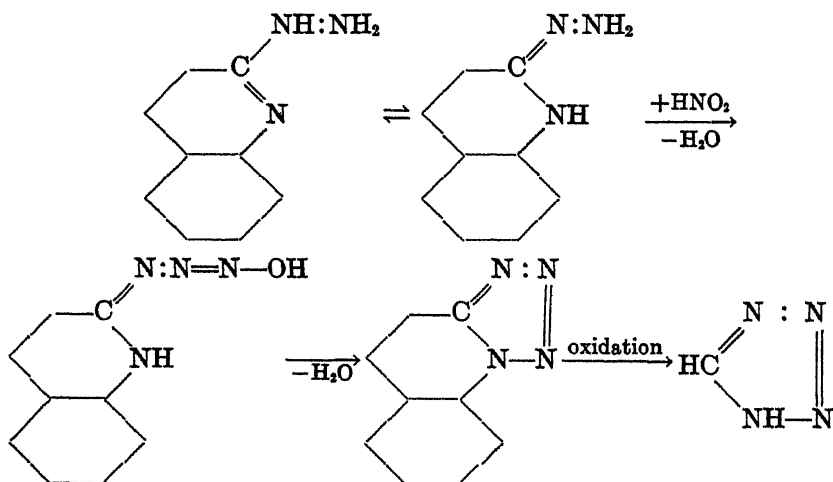
¹³ Cf. footnote 7 concerning the use of the colon and double colon in these formulas.

1. *Preparation.* (a) Tetrazole is obtained in excellent yield by heating hydrazoic acid in alcohol solution with hydrocyanic acid at 100°C. for a period of two or three days (27). Assuming hydrazoic acid and hydrocyanic acid to act respectively as a nitrous acid hydrazide and a formic anammonide, it is reasonable to say that as represented by the equation



an unknown mixed formic acid nitrous acid hydrazide is first formed which, undergoing rearrangement, in principle intramolecular ammonation, passes over into tetrazole.¹⁴

(b) An interesting method for the preparation of tetrazole which involves the action of nitrous acid on a hydrazine derivative, and which furthermore shows the remarkable resistance of the tetrazole ring to the action of oxidizing agents, is due to Marckwald and Meyer (68). By the action of nitrous acid on α -quinolylhydrazine (first and second formulas below), naphhtetrazole, which is represented by the fourth formula, is formed quantitatively. This compound, when treated in a hot dilute acetic acid solution with potassium permanganate, is quantitatively oxidized to tetrazole. The reactions involved may be represented by the scheme

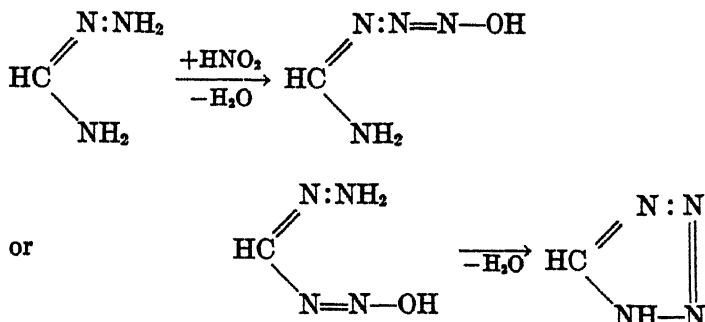


¹⁴ Alternately it may be that hydrocyanic acid, acting as an ammonocarbonous acid, unites with hydrazoic acid to form a carbonous acid azide which arranges to the formic acid azide formulated above.

Since it appears impossible to formulate tetrazole as a derivative of an ammono-

in which the third formula represents an unknown open chain quinoly nitrous acid hydrazide.

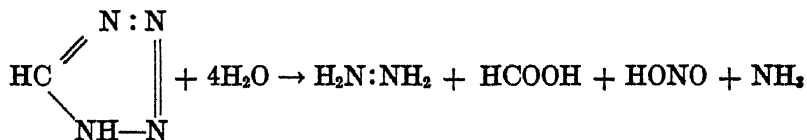
(c) Looking upon tetrazole as a cyclic formic acid nitrous acid hydrazide, it would be reasonable to expect its formation by the interaction of a formic acid hydrazide and nitrous acid, say, as represented by the scheme



While such a reaction is unknown, it does happen that 5-phenyltetrazole has been prepared by the action of nitrous acid on a benzoic acid hydrazide (p. 353), and that 1-phenyltetrazole is formed by the interaction of diformylhydrazine and diazobenzene, which latter compound is a derivative of nitrous acid (p. 354).

2. *Properties.* Tetrazole resists to a remarkable degree the action of acids and alkalis, oxidizing and reducing agents. It is a moderately strong acid, as might be expected of a compound containing an imide group held in common by two acid residues. Its water solution reddens litmus sharply. In solution in water and in liquid ammonia (91) it is a good conductor of electricity. Water solutions of the sodium salt are neutral.

3. *Opening the ring.* (a) Under the action of aqueous hydrochloric acid at 200°C. tetrazole is slowly decomposed to form carbon dioxide, ammonia, and nitrogen (99) instead of undergoing hydrolysis in accordance with the equation

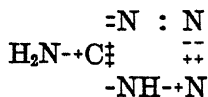


nitric acid, $\text{HN}=\text{N}\equiv\text{N}$, it is important to observe that this method of preparing tetrazole as well as other reactions discussed later, lend substantial support to the view developed elsewhere (41) to the effect that hydrazoic acid is a compound which is capable of acting either as an ammononitric acid or as a nitrous acid hydrazide.

as it might be expected to do on the assumption that it is a formic acid nitrous acid hydrazide. Nitrous acid would of course appear in the form of its anammonide, that is to say, as free nitrogen, as the result of the interaction of nitrous acid and ammonia, while observations made in this laboratory have shown that carbon dioxide and ammonia are formed when sodium formate and hydrazine sulfate are heated together either in the dry state or in solution in water. It follows therefore that the failure of tetrazole to hydrolyze in accordance with the above equation finds a reasonable explanation on the assumption that the formic acid and hydrazine formed interact at the elevated temperature to yield carbon dioxide and ammonia.

4. *Metallic salts.* Salts of sodium, $\text{CHN}_4\text{Na} \cdot \text{H}_2\text{O}$, barium, $(\text{CHN}_4)_2\text{Ba} \cdot 3.5\text{H}_2\text{O}$, and silver, CHN_4Ag , have long been known (89). Strain (91) obtained the ammonium salt, CHN_4NH_4 , by the action of ammonia on tetrazole, and the calcium salt, $(\text{CHN}_4)_2\text{Ca}$, by the action of tetrazole in liquid ammonia solution on metallic calcium and on calcium amide.

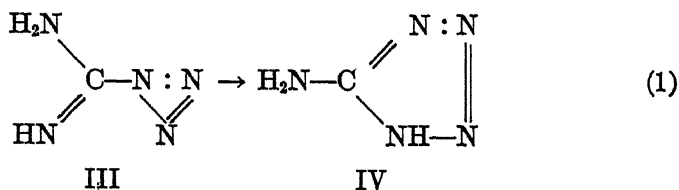
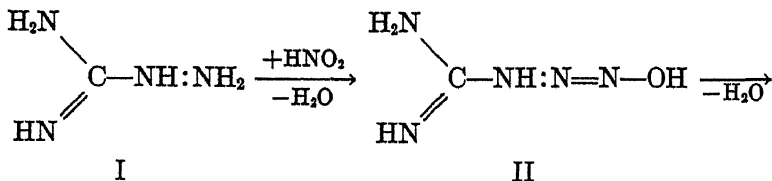
B. 5-Aminotetrazole



This formula represents 5-aminotetrazole as a cyclic carbonic acid nitrous acid hydrazide.

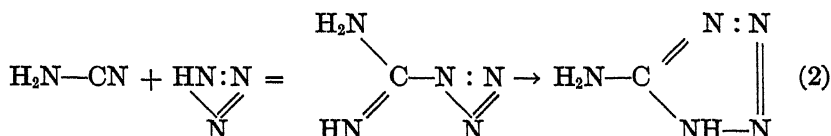
1. *Formation.* Two methods whereby this compound has been made are in harmony with this view concerning its constitution.

(a) By the action of nitrous acid on guanylhiazine guanylazide is formed which latter compound in turn readily rearranges to 5-amino-tetrazole (97). As represented herewith



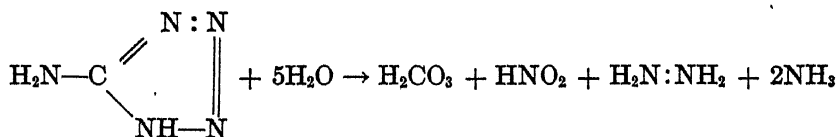
one may say that nitrous acid acts on the carbonic acid hydrazide (I) to form the open chain carbonic acid nitrous acid hydrazide (II), that this compound, known in the form of its nitrate, loses water to form guanylazide (III) which, by intramolecular ammonation of the azide group, isomerizes to 5-aminotetrazole (IV). The compounds II, III, and IV thus appear as carbonic acid nitrous acid hydrazides.

(b) The preparation of 5-aminotetrazole is also readily accomplished by the interaction of hydrazoic acid and cyanamide in water solution (50). Assuming that hydrazoic acid acts as a nitrous acid hydrazide the reactions involved may be represented by the equation



Cyanamide and hydrazoic acid unite to form guanylazide, which, as noted above, readily rearranges to 5-aminotetrazole. The reader will have observed that, as represented by equation 1 above, 5-aminotetrazole is formed by the action of nitrous acid on a carbonic acid hydrazide, while in accordance with equation 2 it results from the interaction of a nitrous acid hydrazide and an ammonocarbonic acid.

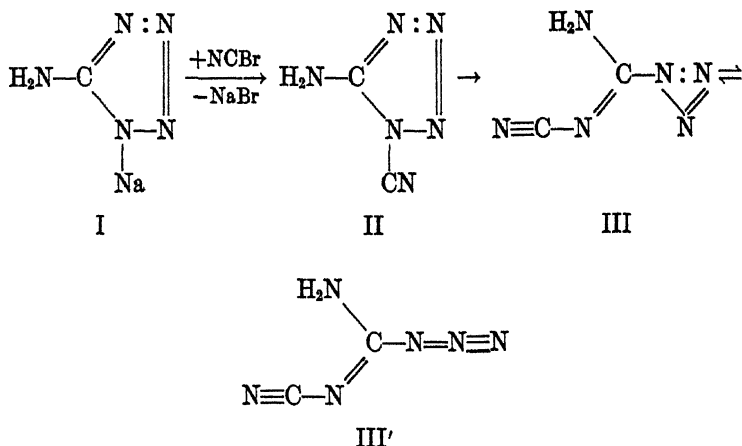
2. *Opening the tetrazole ring.* Regarding 5-aminotetrazole as a mixed hydrazide of carbonic acid and nitrous acid it might be expected that its complete hydrolysis would result in the formation of aquocarbonic acid, nitrous acid, hydrazine, and ammonia in accordance, let us say, with the equation



As a matter of fact, when heated with concentrated hydrochloric acid at temperatures around 200°C., 5-aminotetrazole gives quantitative yields of carbon dioxide, hydrazine, ammonia, and nitrogen (99). The absence of nitrous acid and the appearance of nitrogen among the hydrolytic products is explained when it is recalled that ammonium nitrite readily decomposes to form nitrogen and water. 5-Aminotetrazole hydrolyzes as if it were a carbonic acid nitrous acid hydrazide.

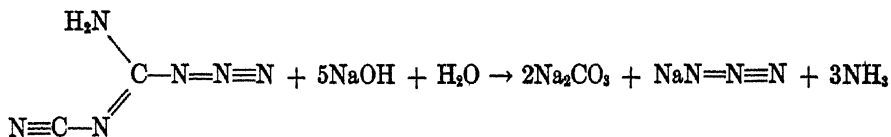
A second method for opening the tetrazole ring is due to Hart (52), who

has shown that dicyanamidazide (III) is formed in accordance with the following equation

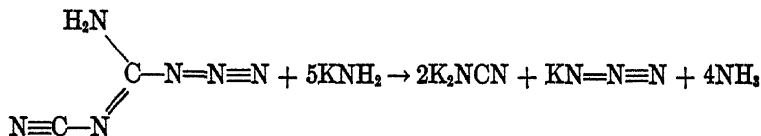


when the sodium salt of 5-aminotetrazole (I) is treated with cyanogen bromide, which is a carbonic acid bromide. The 1-cyano-5-aminotetrazole (II) which one might expect to obtain is for some reason unstable. The ring opens up to form the dicarbonic acid azide represented by the formula III.

Hart observed furthermore (51) that dicyanamidazide is hydrolyzed by the action of warm sodium hydroxide solution to form sodium aquo-carbonate, sodium azide, and ammonia,



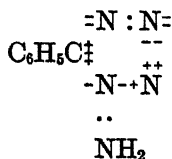
and that it is ammonolyzed to dipotassium cyanamide (an ammonocarbonate), potassium azide (an ammononitrate), and ammonia when warmed with potassium amide in liquid ammonia solution



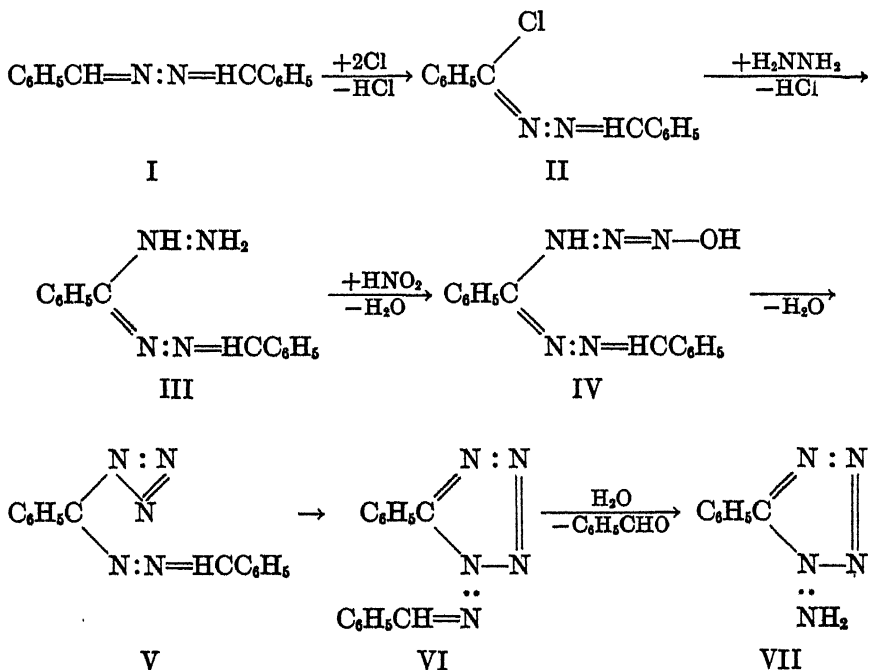
3. *Metallic salts.* Although weaker than tetrazole, 5-aminotetrazole is distinctly an acid of which the salts of silver, $\text{CH}_2\text{N}_4\text{Ag}$, sodium, $\text{CH}_2\text{N}_4\text{Na} \cdot 3\text{H}_2\text{O}$, and barium, $(\text{CH}_2\text{N}_4)_2\text{Ba} \cdot x\text{H}_2\text{O}$, have been prepared

(91). Thiele observed the formation of aluminum, zinc, manganese, cadmium, mercury, cobalt, nickel, iron, and copper salts but did not analyze them.

C. 1-Amino-5-Phenyltetrazole



1-Aminotetrazole, a possible isomer of 5-aminotetrazole, would be a cyclic formic acid nitrous acid hydrazone containing two hydrazine residues. While such a compound is not known its benzoic acid analog, namely 1-amino-5-phenyltetrazole, has been prepared (90). The reactions involved in the formation of this compound, which are in harmony with our assumption that it is a cyclic benzoic acid nitrous acid hydrazone, may be summarized by means of the scheme

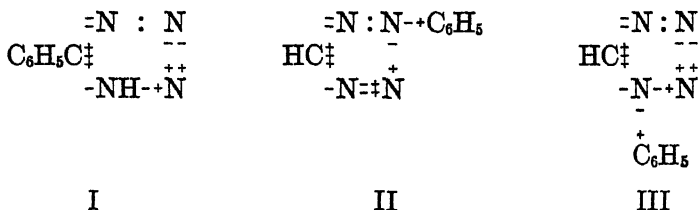


By the action of chlorine on dibenzalhydrazine (I) one of the benzaldehyde groups is augmented to a benzoic acid group, thereby forming II.

This acid chloride reacts with hydrazine to form III (named benzal-benzenyl-hydrazon-hydrazid by Stollé and Hellwerth (90)), which is at the same time a benzoic acid dihydrazide and a benzaldehyde hydrazone. On treating III with nitrous acid the compound IV, containing a nitrous acid group, a benzoic acid group, two hydrazine residues, and a benzaldehyde group is presumably formed. This unknown compound loses water to yield V (benzal-benzhydrazid-azid). Gently heated in alcoholic solution V rearranges to VI, which in turn, under the action of hot aqueous hydrochloric acid, is hydrolyzed to 1-amino-5-phenyltetrazole (VII) and benzaldehyde. It is noted that two molecules of hydrazine and one of nitrous acid enter into the reactions represented above. It is reasonable to say that they persist in the final product. The ready conversion of 1-amino-5-phenyltetrazole into 5-phenyltetrazole by the action of nitrous acid is in agreement with the assumption that the extracyclic NH_2 group is a part of a hydrazine residue. The tetrazole ring in this compound has apparently not been opened.

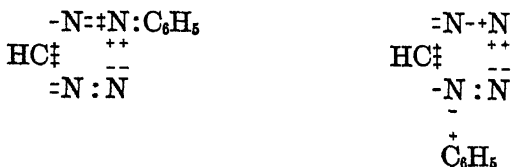
D. Phenyltetrazoles

As will be shown in the following discussion, the methods of preparation of the three known phenyltetrazoles lead logically to the formulas



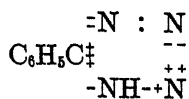
which may be read as representing respectively a benzoic acid nitrous acid hydrazide, a formic acid nitrous acid phenylhydrazide, and a compound which is at the same time a formic acid hydrazide, a nitrous acid hydrazide, and a phenyl ester of a mixed formic nitrous acid. However, beyond the methods whereby they have been synthesized, little or nothing is known which supports the view that the tetrazole ring in these compounds has the constitution represented by the above formulas.

Written as containing formic acid, nitrous acid, and hydrazine residues are two further purely speculative formulas



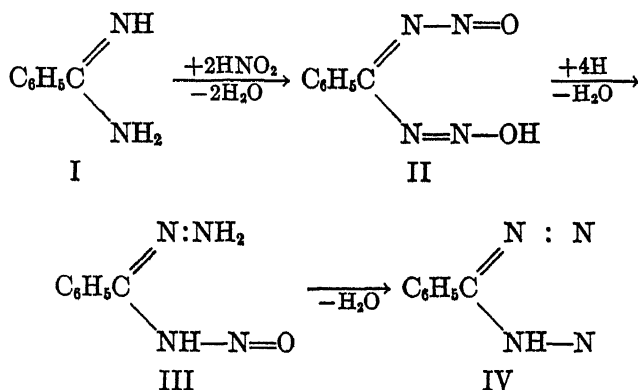
which, while possibly representing compounds not yet prepared, probably rather represent resonance phases, the one of compound II above, the other of III.

E. 5-Phenyltetrazole



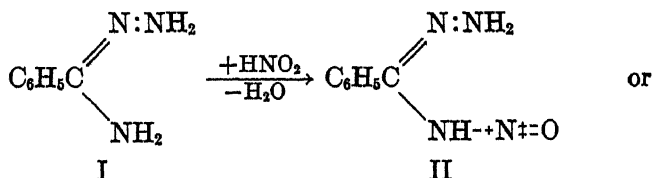
1. *Formation.* The formation of 5-phenyltetrazole from 1-amino-5-phenyltetrazole has already been noted (p. 352). Two further methods for obtaining this compound are here interpreted as showing that it may be regarded as a benzoic acid nitrous acid hydrazide.

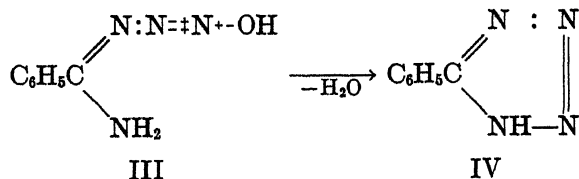
(a) By treating benzamidine with nitrous acid and reducing the resulting diazo compound 5-phenyltetrazole has been obtained (64). The reactions involved may be represented by the scheme



in accordance with which an ammonobenzoic acid (I) is diazotized to the compound II, which was isolated in the form of metallic salts and named benzenyldioxytetrazotic acid. On submitting this compound to the action of sodium amalgam the one or the other of the aquo-ammononitrous acid groups is reduced to a hydrazine group, as shown in the hypothetical formula III which, losing water as the result of the interaction of nitrous acid and hydrazine residues, yields 5-phenyltetrazole (IV).

(b) 5-Phenyltetrazole is formed quantitatively as represented by the scheme



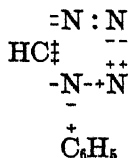


when the benzoic acid hydrazide (I), known in the form of its salts, is treated with nitrous acid (75). By way of II or III, compound I reacts with nitrous acid to form the cyclic benzoic acid nitrous acid hydrazide (IV) which is 5-phenyltetrazole. Whether nitrous acid first converts the amido group in I into a diazo group in II or the hydrazine residue in I into a nitrous acid hydrazide group in III is a matter of no concern in so far as the present argument is concerned. Neither of the compounds represented by formulas II and III is known.

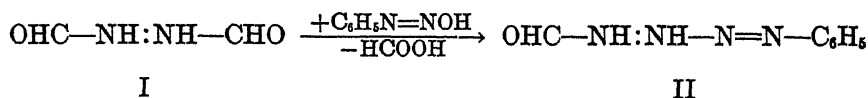
When heated at 200°C. with concentrated hydrochloric acid 5-phenyltetrazole yields nitrogen, carbon dioxide, ammonia, and aniline; these results may be compared with those obtained by the action of hot aqueous hydrochloric acid on tetrazole and on 5-aminotetrazole. The benzoic acid hydrazide part of the molecule obviously undergoes the Lossen rearrangement.

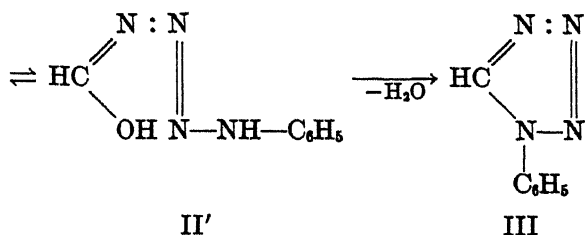
5-Phenyltetrazole is an acid of such strength as sharply to redden litmus. Clemens Lossen (65) prepared an ethyl ester, $\text{C}_7\text{H}_5\text{N}_4\text{C}_2\text{H}_5$, and the potassium, $\text{C}_7\text{H}_5\text{N}_4\text{K}$, barium, $(\text{C}_7\text{H}_5\text{N}_4)_2\text{Ba} \cdot 2\text{H}_2\text{O}$, and silver, $\text{C}_7\text{H}_5\text{N}_4\text{Ag}$, salts. The formation of a considerable number of other metallic salts was observed. They were, however, not analyzed.

F. 1-Phenyltetrazole



This phenyltetrazole has been obtained by the interaction of diformylhydrazine and diazobenzene in alkaline solution (28). Representing the reactions involved by the scheme

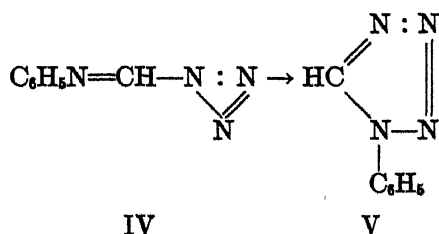
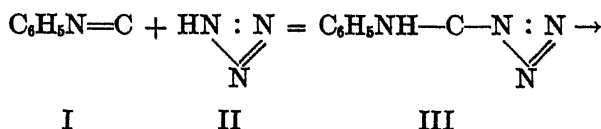




it may be said that an open chain formic acid nitrous acid hydrazide (II, II'), which was isolated but not analyzed, is first formed. When this compound is boiled with aqueous hydrochloric acid it loses water, thereby passing over into the cyclic hydrazide (III), namely, into 1-phenyltetrazole.

Very interesting, in that thereby the tetrazole ring shows its remarkable stability toward hydrolyzing, oxidizing, and reducing agents, is the conversion of 1-phenyltetrazole first, into a nitrophenyltetrazole under the action of fuming nitric acid, second, the reduction of this nitrophenyltetrazole to aminophenyltetrazole, and finally the oxidation of this compound to tetrazole (42).

A second method for the preparation of 1-phenyltetrazole is found in the action of hydrazoic acid on phenylisocyanide (70). Assuming the reactions involved to take place as follows

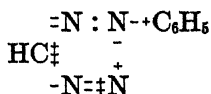


it appears first, that phenyl ammonocarbonite (I) unites with hydrazoic acid (II) to form an unknown carbonous acid ester-azide (III); second, that this compound, after the manner of the transformation of the one tautomer of hydrocyanic acid into the other, rearranges to the formic acid ester-azide¹⁵ (IV); and third, that IV, with the azide group acting as a

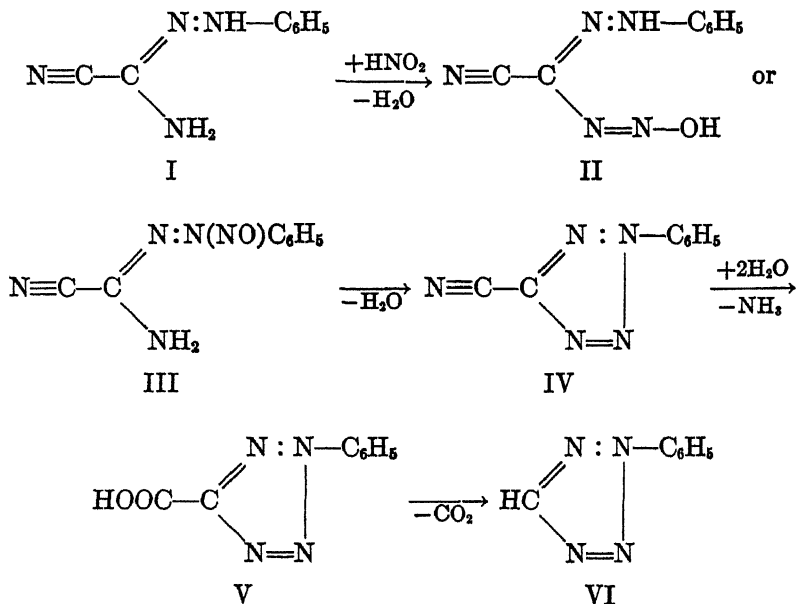
¹⁵ The assumption that compound III is primarily formed is of course highly speculative.

nitrous acid hydrazide group, passes over into 1-phenyltetrazole (V). Being a neutral ester this compound is incapable of forming metallic salts.

G. 2-Phenyltetrazole

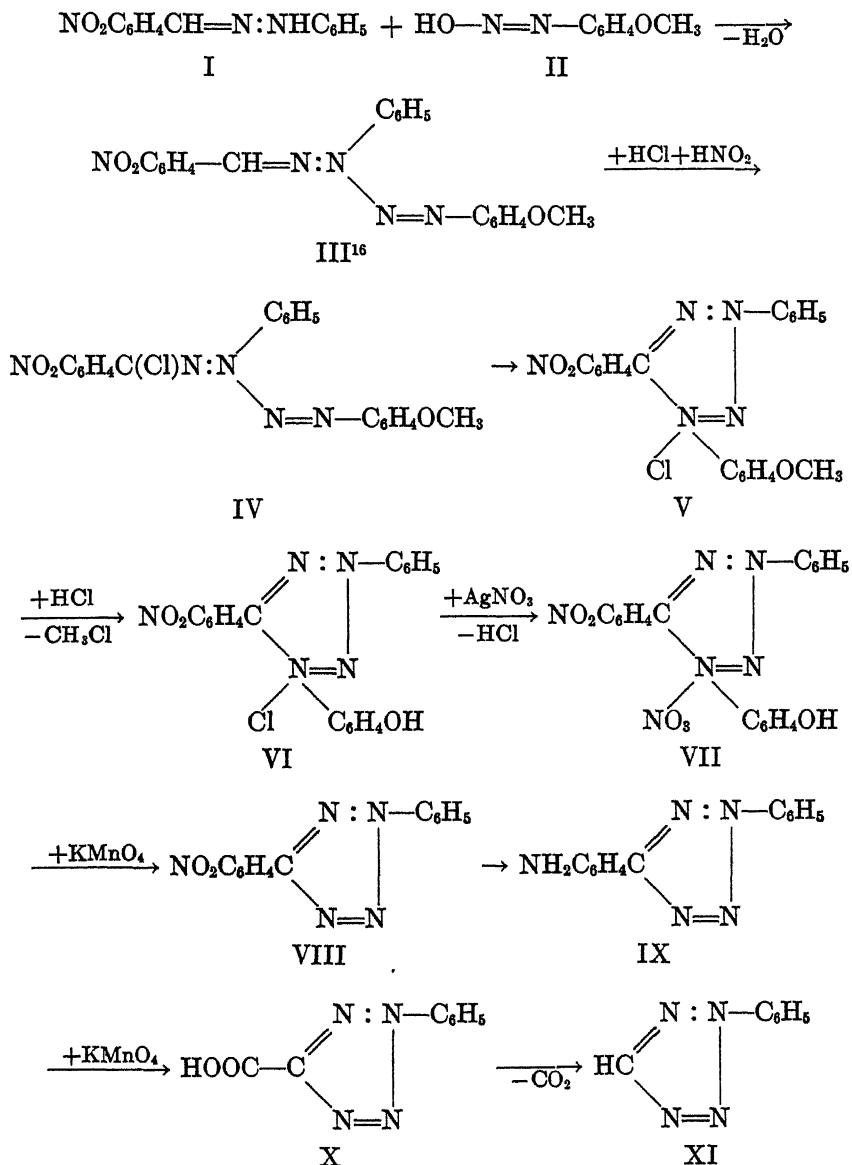


Bladin (12) prepared this compound by means of the successive reactions summarized as follows: Cyanogen, which is the anammonide of oxalic acid, reacts with phenylhydrazine to form a compound (I below), which, in so far as the carbon to phenylhydrazine union is concerned, is a phenyl hydrazide of oxalic acid. By virtue of the presence of the amido group it is at the same time an ammonoöxalic acid. The other carbon atom of the cyanogen remains associated with nitrogen as an oxalic anammonide group. This compound (I) reacts with nitrous acid in accordance with the scheme



to form 2-phenyl-5-cyantetrazole (IV) which, by saponification of the nitrile group to a carboxyl group followed by the elimination of carbon dioxide, is converted into 2-phenyltetrazole (VI). Formulas II and III represent hypothetical compounds. As thus prepared 2-phenyltetrazole appears as a phenylhydrazide of a mixed formic nitrous acid which, containing no acid hydrogen, does not form metallic salts.

Wedekind (101) obtained 2-phenyltetrazole by following the somewhat elaborate sequence of reactions summarized by the scheme



¹⁶ Wedekind used the formula, $\text{NO}_2\text{C}_6\text{H}_4\text{C}(\text{N}-\text{NH}-\text{C}_6\text{H}_5)\text{N}=\text{N}-\text{C}_6\text{H}_4\text{OCH}_3$, to represent this so-called formazyl compound. We venture to give it formula III, which represents it as a derivative of an ammononitrous acid hydrazide, $\text{H}_2\text{N}:\text{NH}-\text{N}=\text{NH}$.

p-Nitrobenzaldehyde phenylhydrazone (I), which is formed by the interaction of *p*-nitrobenzaldehyde and phenylhydrazine, reacts with diazotized *p*-anisidine (II) to form III, which is at the same time a nitrobenzaldehyde hydrazone and a methoxyphenyl nitrous acid hydrazide. This compound, when acted upon by hydrochloric acid and nitrous acid in alcoholic solution, is augmented to the unknown acid chloride (IV), which rearranges to the quaternary salt (V). When heated with fuming hydrochloric acid V yields VI which, under the action of silver nitrate, is converted into the quaternary nitrate (VII). Treated with warm potassium permanganate solution this salt yields 2-phenyl-5-nitrophenyltetrazole (VIII). Reducing agents convert this nitro compound into the amino compound (IX), which under the action of potassium permanganate is augmented to the phenyltetrazolecarboxylic acid (X). Simply upon heating this acid loses carbon dioxide to yield 2-phenyltetrazole (XI). The sequence of reactions may be reasonably interpreted as resulting in the formation of a cyclic formic acid nitrous acid phenylhydrazide.

VI. CONCLUSION

Finally it may be said that the writers by no means claim that all the heterocyclic compounds containing nitrogen in the ring can certainly be formulated in accordance with the hypotheses upon which the many formulas given in this paper are based. Certainly the large majority of the formulas are reasonable enough; others are obviously highly speculative. Even with their shortcomings we deem it worth while to bring our speculations concerning the nature of the heterocyclic nitrogen compounds to the attention of fellow chemists.

REFERENCES

- (1) ANDREOCCHI: Ber. **25**, 225 (1892).
- (1a) AUWERS AND DUESBERG: Ber. **53**, 1179 (1920).
- (2) AUWERS AND SCHAICH: Ber. **54**, 1738, 1750 (1921).
- (3) BALBIANO: Gazz. chim. ital. **18**, II, 258 (1888).
- (4) BALBIANO: Gazz. chim. ital. **19**, II, 689 (1889).
- (5) BALTZER AND VON PECHMANN: Ann. **262**, 320, 322 (1891).
- (6) BAMBERGER AND BERLE: Ann. **273**, 342 (1893).
- (7) BAMBERGER AND DE GRUYTER: Ber. **26**, 3285 (1893).
- (8) BAMBERGER AND LORENZEN: Ann. **273**, 280 (1893).
- (9) BAUER: Ann. **287**, 249 (1895).
- (10) BELL: Ber. **13**, 877 (1884).
- (11) BILTZ AND KREBS: Ann. **391**, 213 (1912).
- (11a) BLADIN: Ber. **18**, 1549 (1885).
- (12) BLADIN: Ber. **18**, 2907 (1885).
- (12a) BLADIN: Ber. **19**, 2598 (1886).
- (12b) BLADIN: Ber. **23**, 1810, 3785 (1890).
- (12c) BLADIN: Ber. **25**, 183, 189, 744 (1892).

- (13) BLADIN: Ber. **26**, 545, 2737 (1893).
- (14) BLAISE AND HOUILLOIN: Compt. rend. **142**, 1543 (1906).
- (15) BUCHNER AND FRITSCH: Ann. **273**, 259 (1893).
- (16) BUCHNER AND PAPENDIECK: Ann. **273**, 234 (1893).
- (17) BÜLOW: Ber. **39**, 2620 (1906).
- (18) CLAISEN: Ber. **36**, 3666 (1903).
- (19) CLAUS AND KOHLSTOCK: Ber. **18**, 1850 (1885).
- (20) CURTIUS, DARAPSKY, AND MÜLLER: Ber. **40**, 837 (1907).
- (21) CURTIUS AND WIRSING: J. prakt. Chem. [2] **50**, 542 (1894).
- (22) DAINS: Ber. **35**, 2503 (1902).
- (23) DIECKMANN AND PLATZ: Ber. **27**, 4644 (1904).
- (24) DIMROTH: Ber. **35**, 1035, 1045 (1902).
- (25) DIMROTH: Ann. **325**, 90 (1904).
- (26) DIMROTH: Ann. **364**, 195, 208 (1909).
- (27) DIMROTH AND FESTER: Ber. **42**, 2223 (1910).
- (28) DIMROTH AND DE MONTMOLLIN: Ber. **43**, 2907 (1910).
- (29) DIMROTH AND TAUB: Ber. **39**, 3912, 3915 (1907).
- (30) FEIGL AND GLEICH: Monatsh. **49**, 392 (1928).
- (31) FEIST AND ARNSTEIN: Ber. **28**, 3176 (1895).
- (32) FERNELIUS AND JOHNSON: J. Chem. Education.
- (33) FISCHER, O.: Ber. **34**, 936 (1901). Cf. MEYER AND JACOBSON: Handbuch der organischen Chemie **2**, 488 (1920).
- (34) FISCHER, O.: J. prakt. Chem. [2] **73**, 423 (1906).
- (35) FISCHER AND KUZEL: Ann. **221**, 280 (1883).
- (36) FISCHER AND PRAUSE: J. prakt. Chem. [2] **77**, 125 (1908).
- (37) FISCHER AND TAFEL: Ann. **227**, 305, 310, 315 (1885).
- (38) FISCHER AND TROSCHKE: Ber. **13**, 706 (1880).
- (39) FRANKE: Monatsh. **20**, 866 (1899).
- (40) FRANKLIN: J. Phys. Chem. **24**, 81 (1920).
- (41) FRANKLIN: The Nitrogen System of Compounds, American Chemical Society Monograph. The Chemical Catalog Co., New York (1934).
- (42) FREUND AND PARADIES: Ber. **34**, 3114 (1901).
- (43) GABRIEL: Ber. **22**, 3338 (1889).
- (44) GATTERMANN AND WICHMANN: Ber. **21**, 1633 (1888).
- (45) GRANDMOUGIN: J. prakt. Chem. [2] **76**, 134 (1907).
- (46) GRASSI-CRISTALDI AND LAMBERTI: Gazz. chim. ital. **25**, I, 225 (1895). Atti accad. Lincei [5] **4**, 169 (1895).
- (47) GRIESS: Ber. **15**, 2195 (1882).
- (48) GROSSMAN: Ber. **22**, 2298 (1889).
- (49) HANTZSCH AND SILBERRAD: Ber. **33**, 85 (1900).
- (50) HANTZSCH AND VAGT: Ann. **314**, 342, 362 (1900).
- (51) HART: Thesis, Stanford University, 1927.
- (52) HART: J. Am. Chem. Soc. **50**, 1925 (1928).
- (53) HELLER: Ber. **37**, 3116 (1904).
- (54) HELLER: Ber. **40**, 118 (1907).
- (55) HOFMANN: Ann. **113**, 251 (1860).
- (56) JACOBSON AND HUBER: Ber. **41**, 664 (1908).
- (57) JAPP: Ber. **15**, 2412, 2417 (1882).
- (58) JAPP AND MOIR: J. Chem. Soc. **77**, 608 (1900).
- (58a) KNORR: German patent, Chem. Zentr. **55**, II, 182 (1894).
- (59) KNORR AND KÖHLER: Ber. **39**, 3257 (1906).

- (60) KNORR AND WEIDEL: Ber. **42**, 3523 (1909).
- (61) KULISCH: Monatsh. **17**, 300 (1896).
- (62) LADENBURG: Ber. **9**, 222 (1876).
- (63) LADENBURG: Ber. **27**, 2952 (1894).
- (64) LOSSEN: Ann. **263**, 73, 96 (1891).
- (65) LOSSEN, CLEMENS: Ann. **263**, 101 (1891).
- (66) MARCHETTI: Gazz. chim. ital. **22**, II, 351, 365 (1892).
- (67) MARCKWALD: Ber. **25**, 2354 (1892).
- (68) MARCKWALD AND MEYER: Ber. **33**, 1885 (1900).
- (69) VON MEYER: J. prakt. Chem. [2] **78**, 497 (1908).
- (70) OLIVERI-MANDALA AND ALGANA: Gazz. chim. ital. **40**, II, 441 (1910).
- (71) PAULING: J. Am. Chem. Soc. **54**, 3577 (1932).
- (72) VON PECHMANN AND BAUER: Ber. **42**, 667, 669, 670 (1909).
- (72a) VON PECHMANN: Ann. **262**, 290 (1891).
- (73) PELLIZZARI: Gazz. chim. ital. **24**, II, 223 (1894).
- (74) PELLIZZARI: Gazz. chim. ital. **39**, I, 520 (1909).
- (75) PINNER: Ann. **297**, 221, 242, 248 (1897).
- (76) PINNER AND SCHWARZ: Ber. **35**, 2444, 2452 (1902).
- (77) RADZISEWSKI: Ber. **10**, 70 (1877).
- (78) RADZISEWSKI: Ber. **15**, 1493 (1882).
- (79) RADZISEWSKI: Ber. **17**, 1289 (1884).
- (80) ROSENGARTEN: Inaugural Dissertation, Jena, 1892.
- (81) ROSENGARTEN: Ann. **279**, 237 (1894).
- (82) RUNG AND BEHREND: Ann. **271**, 34 (1892).
- (82a) SCHÖPPF: Ber. **23**, 1843 (1890).
- (83) SCHWARZ AND GIESE: Ber. **67**, 1108 (1934).
- (84) SHAD: Ber. **26**, 216 (1893).
- (84a) SIDGWICK: The Covalent Link in Chemistry, Ithaca, 1933.
- (85) SILBERRAD: J. Chem. Soc. **77**, 1187 (1900).
- (86) SNAPE AND BROOKE: J. Chem. Soc. **75**, 210 (1889).
- (87) STOLLÉ: Ber. **32**, 797 (1899).
- (87a) STOLLÉ: J. prakt. Chem [2] **69**, 153 (1904).
- (88) STOLLÉ: J. prakt. Chem. [2] **78**, 544 (1908).
- (89) STOLLÉ: Ber. **42**, 1047 (1909).
- (90) STOLLÉ AND HELLWERTH: Ber. **47**, 1140 (1914).
- (91) STRAIN: J. Am. Chem. Soc. **49**, 1566, 1995 (1927).
- (92) STRAIN: J. Am. Chem. Soc. **52**, 1218 (1930).
- (93) STIEGLITZ: J. Am. Chem. Soc. **30**, 1797 (1908).
- (94) TAFEL: Ber. **30**, 250 (1887).
- (95) TAFEL AND STERN: Ber. **33**, 2224 (1900).
- (96) TAFEL AND WASSMUTH: Ber. **40**, 2833 (1907).
- (97) THIELE: Ann. **270**, 1, 54, 57 (1892).
- (98) THIELE AND HEIDENREICH: Ber. **26**, 2598 (1893).
- (99) THIELE AND INGLE: Ann. **287**, 235, 245 (1893).
- (100) THIELE AND MANCHOT: Ann. **303**, 39 (1898).
- (101) WEDEKIND: Ber. **31**, 473, 942 (1898).
- (102) WENZEL: Thesis, Stanford University, 1927.
- (102a) WIRSING: J. prakt. Chem. [2] **50**, 542 (1894).
- (103) WOLFF: Ann. **325**, 134, 152 (1902).

- (104) WOLFF: *Ann.* **394**, 54 (1912).
- (105) WOLFF: *Ann.* **399**, 302 (1913).
- (106) WOLFF AND HALL: *Ber.* **36**, 3612 (1903).
- (106a) WOOD AND BERGSTROM: *J. Am. Chem. Soc.* **55**, 3314 (1932).
- (106b) WOOSTER: *Chem. Rev.* **11**, 23 (1932).
- (107) WUNDT: *Ber.* **11**, 826 (1878).
- (108) WYSS: *Ber.* **10**, 1369 (1877).
- (109) ZINCKE AND LAWSON: *Ann.* **240**, 117 (1887).

THE ELECTRICAL DOUBLE LAYER AND THE STABILITY OF LYOPHOBIC COLLOIDS

E. J. W. VERWEY¹

Eindhoven, Holland

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I. THE ELECTRICAL DOUBLE LAYER

I. INTRODUCTION

Colloid chemistry has learned to distinguish between two types of colloids. First there are the *lyophobic colloids*, which can be flocculated by comparatively small quantities of electrolytes. It is well known that, between 1880 and 1900, investigations of Schulze (113), Linder and Picton (90), and Hardy (54) introduced the concept that the particles of these sols are prevented from sticking together by electrical repulsing forces. Though an exact picture of the significance of the electrical charge of the particles was desirable, this gave qualitatively a plausible explanation of the "stability" of these colloids. Later experiments showed that there is a close connection between the stability and the so-called electrokinetic phenomena. Perrin (102) and Elissasoff (30) studied the electrosmosis, Burton (20) and Powis (103) the cataphoresis, and Kruyt (78) the streaming potentials. Different electrolytes were shown to influence the electrokinetic potential of a surface in a way that is typical for the electrolyte. The same effects were found when the influence of different electrolytes upon the stability of lyophobic colloids was studied.

On the other hand, there is a second type of colloids, which, according to Kruyt (74), Bungenberg de Jong (17), and others, is influenced electrically by electrolytes in the same way; here, however, the mere reduction of the electrokinetic potential (ζ) by electrolytes does not lead to flocculation, on account of a second stabilizing factor. As this factor is determined by the mutual interaction of the particles and the dispersion medium, these sols are mostly called *lyophilic colloids*.

In this article we deal with the electrical properties of colloids, i.e., we

¹ Present address: Natuurkundig Laboratorium der N. V. Philips Gloeilampenfabrieken, Kastanjelaan, Eindhoven.

will not consider the solvation phenomena. Hence our considerations will be valid for lyophobic colloids mainly, and for lyophilic colloids only in special cases.

In his famous article in Graetz's *Handbuch*, von Smoluchowski (114) has treated the total field of electrokinetic phenomena, of the " ζ -potential" derived from them, and the theory of the electrical double layer (1914). Though his conceptions have been extended in several respects by Gouy (50), Stern (116), Frumkin (45), and others, a complete theory of the ζ -potential, and therefore a satisfactory theory of the stability of (lyophobic) colloids, is still lacking. It is well known that Freundlich (33, 34) tried to explain the action of flocculating electrolytes as a neutralization of the charge of the particles by adsorption. This conception has long been the current one. Comparatively recently (1929), however, the theory has been rejected, partly as a consequence of investigations by Freundlich (41) himself. The incorrectness of this theory demonstrated the increasing need of a fundamental theory for the stability of these colloids, i.e., of an exact picture of the mechanism of the mutual interaction between particles and electrolytes.

Meanwhile the number of colloid chemical facts has increased enormously. Yet there is some doubt whether all these data have been gathered with sufficiently reproducible substances, since in many cases the phenomena seem to be very complicated. An important part of this experimental work is handicapped by the circumstance that there is no leading theory generally accepted by all investigators.

In the laboratory of Kruyt (at Utrecht) an extended investigation, with a small number of well-defined substances, was undertaken. The silver halides were chosen as the chief substances of experimental research, since from earlier experience these compounds were expected to be more reproducible and much less complicated than those generally used previously. Indeed, the capillary electrical and colloid chemical investigations revealed a number of new aspects (74a, 74b).

In the present paper the results of these investigations (partly published in Dutch dissertations of Janssen (64), Julien (65), Cysouw (25), and Verwey (130)) will be discussed, together with work of other scientists which contributed to the recent development of our knowledge. In connection with these investigations, the phenomena of the "adsorption of electrolytes" and of the "stability of (lyophobic) colloids" will be subjected to a new theoretical study. On the basis of this study some general lines of thought will be developed, which, in our opinion, have to be drawn distinctly in all colloid chemical work, in order to give to this field of research its necessary theoretical background.

II. COLLOID ELECTROLYTE OR TWO-PHASE SYSTEM?²

The general treatment and the subdivision of our subject may be elucidated by a preliminary remark. The lyophobic colloids constitute a difficult borderline case between two fields studied reasonably well: (1) the molecular disperse system of a solution of an electrolyte, and (2) the two-phase system solid-solution with a single continuous and flat boundary layer. In our study of the laws of colloids both extremities may function as a starting point for our considerations. Then, extending our reasoning to the case of a definite colloidal system as a next approximation, we have to make the necessary corrections.

In the first place we can take colloids as electrolytes, and study them by the well-known methods of electrochemistry. This way is chosen by Zsigmondy (142) and especially by Pauli (100). The charged particles are called "colloid ions," and the ionic spheres of opposite charge around them constitute the so-called "counter-ions." This nomenclature, and the electrochemical study, is advantageous in many respects. It is not sufficient, however. The main problem of colloid chemistry, the stability of the sols, does not come out to advantage in the "electrochemistry of colloids." Its particular difficulty is the asymmetrical character of these "electrolytes." The "valency" of the colloid ion generally amounts to from some thousand to several million unit charges per particle. So the limit laws of Debye-Hückel (27) do not hold any more.

Freundlich (33), Kruyt (74), and others chose the other method, and started from the *flat double layer*. For our purpose, too, this is the only possibility. Only occasionally shall we consider the corrections for a strong curvature of this boundary layer, i.e., for the case when the particles are extremely small. For the present our reasoning will be restricted to systems of low dispersity; hence the number of molecules (ions) in the surface of our particles is assumed to be negligibly small as compared with the total number in these particles.

In the next sections of this paper we shall deal with the electrical double layer and its properties. In Part II our considerations will be applied to the problem of the stability of lyophobic colloids. In Part I we are therefore especially interested in systems where the conditions are much like those in colloidal lyophobic solutions. This is the reason why we restrict ourselves to systems in which one of the phases is a solution of electrolytes.

² *Note added in proof:* Meanwhile a valuable contribution to the problem of this section has been made by a General Discussion on Colloidal Electrolytes held by the Faraday Society (Gurney and Jackson, London, January, 1935). See in particular the papers of Wo. Pauli, H. R. Kruyt, G. S. Hartley, and A. J. Rabinovitch and V. A. Kargin.

As a rule the double layer at gas-solid or gas-liquid interfaces (which is governed by quite different laws) is left out of the discussion.

III. THE STRUCTURE OF THE DOUBLE LAYER

The potential difference between two phases manifests itself in a potential drop in the neighborhood of the boundary layer. In part it is effected by oriented and polarized molecules or (and) ions, i.e., by a shift of electrical charge within one phase. Generally, however, a double layer of free charges contributes also to the potential drop. This double layer consists of two space charges of opposite sign in the surface of both phases. Let us consider, for instance, silver iodide crystal in contact with a dilute solution of electrolytes. When equilibrium is reached, the silver iodide lattice may contain in its surface a number of iodide ions in excess, and the silver iodide thus will be charged negatively. Then, in the immediate neighborhood of the surface, the solution must contain an equal number of cations in excess.

In older pictures of the double layer (e.g., that of Perrin (102)), the latter is assumed to be built up by two "mono-ionic" layers of opposite charges touching each other in the boundary plane. This very simple picture, which obviously neglects the thermal agitation of the ions, is often (but unjustly, according to Janssen (64)) ascribed to von Helmholtz (56). The modern conception has been given by Gouy (1910). (Afterwards similar considerations were held by Chapman (22), Herzfeld (58), and Debye and Hückel (27).) Gouy calculates the partition of the charges in the outer layer on the side of the solution. On account of their kinetic agitation the ions of this layer (in our example the cations) partially escape from the attracting forces of the charge of the surface; on the other hand, some anions will succeed in getting into the first layers. This equilibrium of attracting, repelling, and kinetic forces is calculated by Gouy on the assumption that both ions have negligible dimensions. The number of cations and anions, as a function of the distance from the surface, is then reproduced schematically by figure 1; the shaded surface is a measure of the total charge of the outer layer.

According to this theory the total potential drop caused by the double layer occurs in the outer "diffuse" layer. Moreover, one should expect that the whole outer layer may shift against the surface, e.g., in an electrical field, and thus give rise to electrophoresis, etc. This is contrary to experience. von Smoluchowski (114) has pointed out (1914), and afterwards Freundlich (33) and Gyemant (51) also, that the ζ -potential calculated from electrokinetic measurements is not identical with the total potential drop; both potentials depend on the concentration and the nature of the electrolytes in the solution in a fundamentally different way. The

theory has been improved by Stern (116), who takes into account the size and specific properties of the ions. According to him only part of the ions of the outer layer make themselves free from the attracting surface. Thus the total liquid charge is divided into two parts: the charge of the ions that remain attached to the surface, and a part built up by the free and mobile ions of the diffuse layer. The adhering ions are held by purely electrostatic and by specific forces. In connection with the latter a specific "adsorption potential" is given to each ion. The introduction of the adsorption potentials rather complicates Stern's equations, but in some cases they can be neglected; in which case Stern's picture is an adequate and valuable approximation of the state of affairs in the double layer.

Recently the theory of Gouy has been worked out by Janssen in a somewhat different direction. Janssen (64) argues that the mobility of

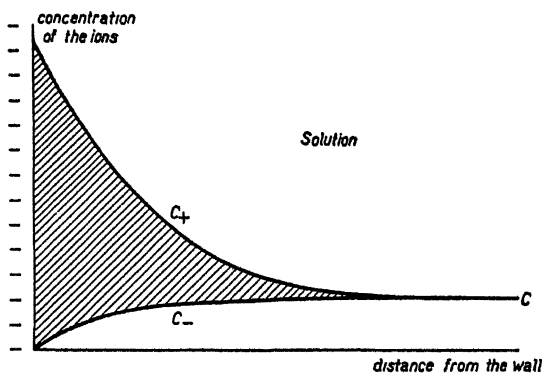


FIG. 1. Distribution of positive and negative ions in the neighborhood of a negative surface ("diffuse layer").

the liquid in the neighborhood of the surface is lowered as a consequence of solvation powers (attraction and orientation of water molecules). He assumes a layer of liquid attached to the surface. This conception may also explain the difference between total potential drop and ζ -potential.

Though von Smoluchowski apparently was not acquainted with Gouy's paper he also assumes an outer charge reaching some distance into the solution. However, according to him the potential drops continuously in both phases, i.e., in our example, part of the total potential occurs in the silver iodide phase. This has been confirmed by calculations by the author (127) from experimental data on the dialyzed silver iodide sol, which is the only case for which sufficient data are as yet available. The result of the calculation is shown schematically in figure 2. The part, ψ , of the total potential drop that falls in the liquid phase is again divided

into two parts: one in the attached layer (Stern-Janssen) and the other in the diffuse layer (Gouy).³

The conditions of figure 2, though realized in our case, are only of a simple type. Eventually the slope of the potential may be more complicated, e.g., the potential curve may contain a maximum or minimum, as will be stated later. But even if such complications are neglected for the present, it is an extremely difficult problem to find a relation between the different parts of the total potential drop. Yet this is highly important for colloid chemistry, since the stability of lyophobic sols depends solely or mainly on the ζ -potential of the particles, and this ζ -potential is clearly seen to be connected in a way with the potential drop in other parts of the double layer.

Hence, in order to be able to predict the magnitude of this ζ -potential in a given case, and its variations with the concentration of different

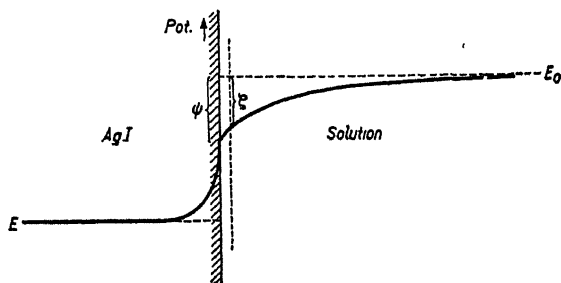


FIG. 2. Curve for the potential, perpendicular to the surface silver iodide-solution, in case of a dialyzed silver iodide sol.

electrolytes, we must study the slope of the potential within the entire double layer. Nevertheless it may be useful, as a simplifying approximation, to consider only the diffuse outer layer, assuming for instance that the charge of this layer (η_2) is constant. It will be shown in Part II that this very simple picture, with the aid of Gouy's theory, already helps us to understand several aspects of the general behavior of lyophobic colloids.

Strictly speaking, the assumption of an electrophoretic charge, which is independent of the concentration of electrolytes, is not correct. This, for instance, is shown in Stern's theory. For rather concentrated solutions only a small fraction of the outer ions will be in the mobile layer ($\eta_1 > \eta_2$), since a large number of collisions favor a high "adsorption." For extremely small concentrations of the electrolyte, however, the theory of Stern finally becomes practically identical with the picture of Gouy (hence

³ The corresponding charges will be denoted throughout by η_1 and η_2 , respectively.

$\eta_1 < \eta_2$). Comparing, as usual, the double layer with an electrical condenser, we may state that in concentrated solutions its capacity will not differ much from the capacity of the attached part. For more dilute solutions the mean distance between outer and inner charge increases, since an increasing part of the outer layer is "diffuse." Thus

$$C = \frac{D}{4\pi d}$$

decreases (C = capacity, D = dielectric constant, d = distance between the charges). This is actually seen from Gouy's data on d/D , calculated from the electrocapillary curve of mercury. This quotient (in 10^{-8} cm.) is for two electrolytes as follows:

	<i>1 normal</i>	<i>0.1 normal</i>	<i>0.01 normal</i>
Potassium nitrate.....	0.393	0.451	0.500
Sodium acetate.....	0.422	0.467	0.501

From such data we conclude that d/D for the attached layer is of the order 0.4×10^{-8} . The corresponding capacity is about $20\mu F$ per square centimeter. These values are determined by the molecular dimensions and the mean dielectric constant in the double layer. Here some difficulties arise. We must keep in mind that a "dielectric constant" can only be defined distinctly for a volume element which is large in comparison with the size of ions and molecules. Hence we cannot speak of the dielectric constant of the double layer, since this very constant changes there abruptly in a distance of a few molecular dimensions. We can discuss only the electrical polarizability of the ions and molecules present; the average value is determined by the polarizabilities of the constituent ions, of the surface, and of the water molecules in the outer layer. Since the latter are greatly immobilized by the electric fields of the former (hydration), we need to consider practically only the atomic and "optical" polarization and not the orientation polarization, i.e., we must take not the high value $D = 80$ (dielectric constant of pure water), but a value not much larger than 2.

Assuming that the distance of both charges is of the order of 3×10^{-8} cm. (average sum of two ionic radii), we calculate from Gouy's data a "dielectric constant" of the double layer $D = 8$. This is of the expected order of magnitude.

It may be stated here that a general difficulty in the current theory of the double layer is that its special molecular mechanism is generally neglected. Only the partition of charges in a direction perpendicular to the boundary layer is considered; the electric charge is treated mathematically as a continuous one, distributed homogeneously over the surface.

We shall see that actually the conditions often differ considerably from these assumptions. The neglect of all potential gradients along the boundary surface is, to be sure, sometimes allowed, especially in the diffuse outer layer where the time average no longer contains the fine structure of the charges. But in the neighborhood of the boundary layer the discontinuous and possibly irregular distribution of the charges becomes of considerable importance.

The problem we have to deal with is, of course, simple for the double layer between mercury and solution, or between air and solution. Here the ions move freely over the surface, and all points of it are equivalent. It is easy to conclude from the capacity of the double layer calculated above that at the most only a small per cent of the mercury surface is covered with ions.

The phenomena for the system solid-gas are already more complicated. In particular, the boundary layer of solids with a polar lattice (salts) has been studied, e.g., by Langmuir (88), and recently by de Boer (8) and his coworkers. The latter, for instance, examined the adsorption of iodine, cesium, or volatile organic compounds by a thin sublimed layer of calcium fluoride. First they concluded that these layers contained superficially only fluoride ions, thus showing that the surface of the salt layers consists of 111 planes. This statement was confirmed by electron diffraction experiments (Burgers and Dippel (21)). Now on each fluoride ion in the surface, i.e., on each lattice point, maximally one atom of hydrogen, or one-half a molecule of iodine, is adsorbed. A molecule of *p*-nitrophenol is probably adsorbed on every fourth fluoride ion, but then a second layer of molecules is adsorbed on the first one through weaker forces of the van der Waals type. In the adsorption of cesium atoms the surface is covered by several layers of these atoms. Hence in all cases, though they differ among each other, the adsorption occurs in a definite way at distinct adsorption centers. Optical investigation of slightly covered salt layers (de Boer and Custers (10)) and the study of the sintering process of these sublimed layers (de Boer and Dippel) proved, moreover, that these adsorption centers must be divided into active spots and less active ones; on the former adsorption takes place more easily and with a larger gain of energy. Hence the properties of the lattice are again found to some extent in the adsorbed or double layer.

We were led to similar conclusions by our investigations with the silver iodide sol, although here we deal with a system where water molecules are also present (Verwey and Kruyt (123, 124)).

A first result of this work was that with a dialyzed (negative) silver iodide sol the surface density of the charge is extremely small. We found, for instance, values ten times as small as the charge density (per square

centimeter) for mercury-solution. With the strong "aging" of these sols this value still decreases. A detailed study of these aging phenomena, analytically and with the aid of x-rays, led to the conclusion that on the silver iodide particles the charging iodide ions are present only at certain active spots. All kinds of irregularities, cavities, lattice distortions, etc., of the silver iodide surface may function as such. These preferred places will thus be of the same nature as Smekal's (113a) "Lockerstellen" or H. S. Taylor's (117) active spots on catalysts. It seems that the undisturbed crystal faces do not contribute to the double layer. This is in accordance with modern conceptions of crystal growth (Kossel, Stransky; cf. van Arkel and de Boer (5)). It also explains the abnormally low values of the charge of the double layer per square centimeter of surface.

The aging process therefore consists in the first place of a perfecting of the particles. Immediately after the precipitation the small crystals of silver iodide have a very imperfect lattice with many active spots. Upon aging, such an irregularly formed crystal gradually transforms into a more perfect one, with fewer places that are able to take up iodide ions. Partially also a coarsening of the sols occurs, but with moderate aging this process practically does not yet appear in the case of dialyzed silver iodide sols.

Recently similar aging processes were studied with several other precipitates by Kolthoff, Rosenblum, and Sandell (70, 71, 72), in connection with Kolthoff's investigations of coprecipitation and the physical properties of analytical precipitates. They also found that precipitates of lead sulfate, etc., are subject to enormous changes in their lattice structure during the first period of their existence.

We see therefore that in the case of silver iodide and probably also in other cases the charge is not distributed homogeneously over the surface, and that the double layer is concentrated more and more in a small number of (active) spots. Hence there is actually a strong deviation from the homogeneous and continuous distribution of the charge assumed in the computations of Gouy, Stern, and others.

de Boer and Veenemans (12), in recent investigations regarding the adsorption of the atoms of volatile metals by metal surfaces, have considered the influence of a discontinuous distribution of the charge upon the slope of the potential within the double layer. If the plates of a condenser of infinite surface are charged by two continuous charges, the field at both sides of the condenser is zero (figure 3). If, however, the plates are covered with a number of concrete charges at comparatively large distances from each other (figure 4), only part of the average potential drop occurs between both layers. The discontinuous distribution of the charge is the reason for existence of residual fields outside the condenser.

The actual existence of these residual fields of a double layer of the type of figure 4 has been proved by the experiments of deBoer and Veenemans.

If, moreover, the charges are distributed irregularly over the surface, this factor must *a fortiori* be taken into account. The consequence is that part of the total potential drop must occur *within* the silver iodide

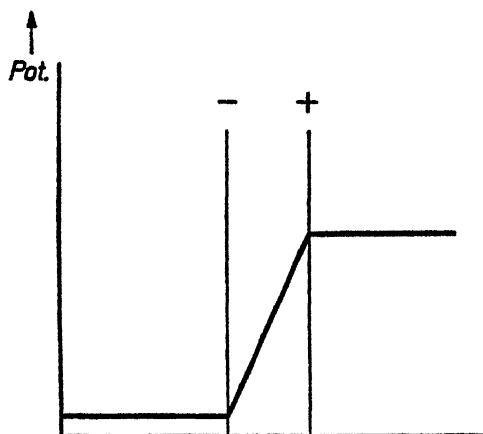


FIG. 3. Condenser with continuous charge distribution

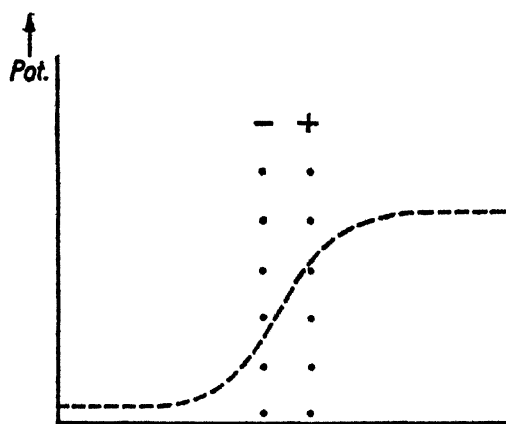


FIG. 4. Condenser with discontinuous charges

phase. This is the plausible explanation of the left-hand part of the potential curve of figure 2, calculated by the author from experimental data on the silver iodide sols.

From this we see the importance of a topographical study of the double

layer. In most cases, however, we do not know anything about it. We cannot even account for the extremely high values of the apparent capacity of the double layer found for many sols. We calculated this capacity (126, 130) for arsenic trisulfide, gold, and silver sols, and also for etched silver, from data of Pauli and Valko and of Proskurnin and Frumkin (46). We found values several hundred times larger than the double layer capacity of 1 square centimeter of mercury-solution. The surface density of the charge seems to be much larger even than that of a closely packed layer of ions. In these cases obviously some complication exists. For the same reason there is an unexplained discrepancy between the free charges calculated from the conductivity of the sols and from their electrokinetic potentials, respectively. The first may be found to be about 1000 times as large as the latter. Only in the case of the dialyzed silver iodide sol, where the charge of a particle is extremely small, is this discrepancy not found. This is another argument why the silver halides, in particular, silver iodide, are more simple substances for colloidal research than the usual sols.

IV. THE FORMATION OF THE DOUBLE LAYER

Suppose we bring electrolytically conducting phases in contact with each other, e.g., silver iodide and an aqueous solution of an electrolyte. How, then, is a double layer formed? We assume that the solution has been previously saturated with silver iodide; for this, indeed, a very small amount of silver iodide is sufficient, since the solubility at room temperature is only 10^{-8} equivalent per liter. The concentration of silver and iodide ions may still vary within wide ranges; always, however, the ionic product $c_{\text{Ag}^+} \times c_{\text{I}^-} = 10^{-16}$.

Both phases contain silver ions, and generally the thermodynamic potentials of these ions are not the same in the silver iodide and in the solution. Hence silver ions will move in one direction, say from the silver iodide to the solution, and cross the boundary layer. Iodide ions move in the opposite direction, since the ionic product in the solution must remain constant. By this transportation of ions the silver iodide phase is going to contain an excessive amount of iodide ions, i.e., the silver iodide is charged negatively. Further transportation will soon be prevented by the charge thus formed. For electrostatic reasons this negative charge, as the equal positive charge in the solution, is localized in the neighborhood of the boundary layer. The potential drop caused by the electrical double layer thus formed occurs in the same region. Thus we may state that the potential difference between silver iodide and solution is determined by a distribution of common ions (silver ions or iodide ions; Lange (82, 87) calls them potential-determining ions) over both phases.

When equilibrium is reached, according to Nernst, van Laar (81), and Haber and Beutner (52a),

$$E = \epsilon + \frac{RT}{F} \ln c_{\text{Ag}^+} \quad (1)$$

is valid, or

$$E = \epsilon' - \frac{RT}{F} \ln c_{\text{I}^-}$$

So the total potential drop in the double layer, E , depends only on the concentration of the potential-determining ions. However, it is not necessarily true that E is entirely due to a transportation of charges from one phase to the other. For a definite c_{Ag^+} (or c_{I^-}) in the solution such a transportation will not be needed in order to establish an equilibrium; this corresponds to the concentration for which the charge of the ionic double layer is zero. In this "zero point of the charge" the value of E is generally not zero ($E = E_0$). This remaining potential difference E_0 is attributed to the orientation of the water molecules (electric dipoles) in the boundary layer or the mutual polarization of lattice ions, water molecules, etc. Potential differences of this kind can be measured only with difficulty. (χ -potentials, after Lange). Therefore E_0 and thus the absolute value of E is unknown. For our purpose, however, only the changes of E are important. There is some evidence that χ varies only slightly with E (Andauer and Lange (3)). As a first approximation we will assume that there is a simple superposition of the χ -field (in this event equal to E_0) and the field of the double layer. In this ideal case changes of E are entirely supported by a transportation of ions through the boundary layer; the proper potential of the ionic double layer is $E - E_0$.

The formation of the double layer manifests itself as an "adsorption." If silver iodide is charged negatively by a solution of hydriodic acid, a number of iodide ions go from the solution into the surface of the silver iodide. Only an extremely small number of silver ions are transported in the reverse direction, since the concentration of the latter in the hydriodic acid solution is very small and can increase only slightly. Hence the ionic transport is practically unidirectional. The iodide ions adsorbed are accompanied by an equivalent amount of hydrogen ions. These ions remain in the solution phase and constitute the outer charge of the double layer. Hence, as a whole, a certain amount of hydriodic acid is taken from the solution and "adsorbed" by the silver iodide in order to build up the double layer.

At the other side of the zero point of the charge, in a solution with a sufficiently great value for the concentration of silver ions, the formation of a positive double layer takes place in a similar way by the adsorption of, say, silver nitrate.

For a constant capacity of the double layer the amount of iodide ion (silver ion) that is taken up by 1 gram of silver iodide, x , is proportional to $E - E_0$, hence

$$\text{or } \left. \begin{aligned} x &= k_1 + k_2 \log c \\ \frac{dx}{d \log c} &= \text{constant} \end{aligned} \right\} \quad (2)$$

These equations will generally hold for any kind of potential-determining electrolytes, hence for the "adsorption" of silver ion by silver, of mercuric ion (Hg_2^{++}) by mercury, of hydroxide ion or hydrogen ion by glass, etc. According to Lange and Berger (82, 84) equation 2 is valid for a precipitate of silver iodide between c_{Ag^+} (or c_{I^-}) = 10^{-9} to 10^{-7} , and they prove the probability of this law for some other cases (see also Lange and Andauer (2)). In our own experiments (125) we have measured the "adsorption" of potassium iodide by dialyzed silver iodide sols, and found that equation 2 actually holds for iodide-ion concentrations up to 10^{-4} equivalent per liter. (In these sols c_{I^-} is about 10^{-7} equivalent per liter.) We were also able to determine the amount of iodide ion that was already present in the double layer of the sols (123, 125), and from this we could estimate by an extrapolation with the aid of equation 2 the value of c_{I^-} for the zero point of the charge ($E = E_0$). We found that the silver iodide of these sols is uncharged when it is in equilibrium with a solution of about 10^{-6} *N* silver ion (or $c_{\text{I}^-} = 10^{-10}$). The zero point of the charge coincides therefore with the zero point of the electrokinetic potential found earlier by Kruyt and van der Willigen (80) and by Lange and Crane (85). The negative charge of silver iodide in pure water is therefore due to the excess of iodide ion it "adsorbs," and is not caused by a specific adsorption of hydroxide ion as has been generally assumed hitherto. The tendency of the iodide ion to go from the solution into the silver iodide phase is so much greater than that of the silver ions that a 10,000-fold excess of the latter is necessary in order to reach the point where they counterbalance each other.

These data are only valid for the case of our dialyzed silver iodide sols, prepared in a definite way; our sols were electrodialed immediately after preparation and then concentrated by "electrodecantation" after Pauli (100a). As the aging process proceeds only very slowly after the removal of the free iodide ion (cf. Part II, section I), the degree of aging of these sols did not vary much. The size of the particles was about 40 m μ . Julien

(65) has found that large crystals of silver iodide (and other halides of silver), e.g. when crystallized from molten silver iodide, cannot be charged electrokinetically positive by even 0.001 *N* silver nitrate solution. Apparently the zero point of the electrokinetic charge (Julien measured streaming potentials and electrosmosis) and probably also the zero point of the total charge depends chiefly on the nature of the silver iodide; in the dialyzed sols the charge is reversed by 10^{-6} *N* silver nitrate, but coarse crystals of silver iodide are still negative in 10^{-3} *N* silver nitrate. Julien also studied the change of the properties of fresh precipitates when they were subjected to an aging and coarsening process in a solution of 0.001 *N* silver nitrate. In this solution the fresh precipitate of silver bromide is positive, but the charge decreases continually with the time, and after several hours turns negative. With silver iodide the same inversion was observed, but, in accordance with its lower solubility, the change proceeded much more slowly. With better and larger crystals, therefore, the zero point of the charge is shifted considerably to higher silver-ion concentrations, and becomes more and more asymmetrical. The equilibrium of the distribution of the potential-determining ions over silver iodide and solution shifts in such a way that the affinity of the iodide ions for the silver iodide increases continually.⁴

The investigations of Julien may warn us that it is dangerous to apply results gained from macroscopic objects to submicroscopic systems.

Several measurements of "adsorption" of electrolytes do not deal with adsorption in the proper sense, but are in reality measurements of the formation of the double layer by potential-determining electrolytes. Beekley and Taylor (7), for instance, determined the "adsorption" of silver salts by silver iodide. Probably we must explain their data by a definite influence of the size and the polarizability of the anion (in this case the outer ion of the double layer) upon the capacity of the double layer. The experiments of Fajans and Erdey-Grúz (32), too, partly deal with "adsorptions" of the type considered in this section. It must be stressed that this also holds for their qualitative measurements of the "adsorption" of potassium bromide, potassium chloride, and potassium thiocyanate by silver iodide. As silver bromide, etc., forms mixed crystals with silver iodide, the ions Br^- , Cl^- , SCN^- are all potential-determining ions for the case of silver iodide-solution. For these ions will be distributed over both phases. Imre's (61) measurements of the "adsorption" of lead ion (ThB^{++}) by barium sulfate deal with a similar case. His data seem

⁴ *Note added in proof:* Similar phenomena have been observed recently by H. R. Kruyt and R. Ruyssen (Proc. Acad. Sci. Amsterdam 37, 624 (1934)) in studying the streaming potentials of both large and small crystals of barium sulfate in various solutions.

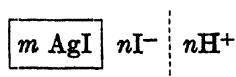
to indicate that in the first moment the lead ions are distributed over the solution and the surface layer of the barium sulfate crystals; gradually, however, the lead ions diffuse into the barium sulfate lattice, substituting the isomorphous barium ions, until a definite ratio of $\text{Pb}^{++}:\text{Ba}^{++}$ is reached. Kolthoff (69) also interpreted Imre's results as a formation of mixed crystals.

We found several similar examples in the chemical literature where these phenomena were insufficiently distinguished from real adsorption and other phenomena. But the cases treated above probably prove sufficiently that a better interpretation and a clear insight will be gained only if one takes into account the special rules holding for this type of "adsorption," i.e., the fundamental fact that these potential-determining electrolytes are required for the formation of the double layer.

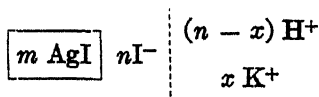
V. EXCHANGE OF COUNTER-IONS

We next examine the interactions between a double layer, once formed, and other (indifferent) electrolytes added to the system. The most general and simple of them is the exchange of counter-ions.

We have, for example, silver iodide negatively charged, which may be written:



and suppose that an indifferent electrolyte, say potassium nitrate, is added to the solution. Apart from other actions, neglected for the time, part of the potassium ions will penetrate into the outer part of the double layer. Here the positive hydrogen ions are cumulated. These potassium ions, positive ions too, may take the function of supporting the positive space charge from the hydrogen ions, allowing an equivalent amount of the latter to move back into the bulk of the solution. When equilibrium is reached, i.e., when in a sufficiently long time equal amounts of potassium ion enter the double layer and leave it, a quantity, x , of potassium ions has been "adsorbed," but an equal quantity of hydrogen ions has been given back to the solution:

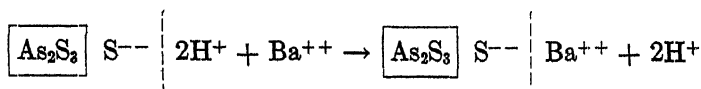


The total concentrations of electrolyte in the double layer and in the solution are not altered; only an exchange of counter-ions has taken place.

This type of exchange is a general phenomenon, occurring in almost

every case where a solution of an electrolyte is brought in contact with a surface. Always where the counter-ion of the double layer and the equally charged ion of an electrolyte added to the system do not happen to be identical, an exchange occurs. A double layer is always present in a sol (otherwise the sol would not exist) in practically all precipitates, adsorbents, etc. In section IV we have stated that even a thoroughly washed silver iodide precipitate still contains a double layer, hence exchangeable counter-ions. Silver iodide, and presumably silver bromide and other precipitates, when in equilibrium with pure water (Lange and Crane (85) claim 80-fold washing is necessary to reach this) are certainly not "Äquivalenzkörper" (Fajans), for only when the zero point of the charge and the equivalence point in the solution ($c_{Ag^+} = c_I^-$, etc.) happen to coincide is the precipitate uncharged. Also charcoal, even when ash-free, contains a double layer. Interesting experiments of Frumkin and coworkers (44) revealed that here hydrogen ion and hydroxide ion are the potential-determining ions. This explains that a "hydrolytic adsorption" was often found (Kolthoff (68) and others), it actually being an exchange.

Historically remarkable is an old study of Whitney and Ober (138), which has been interpreted erroneously by many colloid chemists. These investigators were apparently aware of their observing something else than an "adsorption," when they studied "the composition of the precipitate" obtained after the flocculation of an arsenic trisulfide sol by barium, calcium, strontium, and potassium salts. They stated that the precipitate had a constant composition and were of the opinion that equivalent amounts of barium hydroxide, etc., were coprecipitated. How this "precipitation" of a basic hydroxide could be produced, together with the liberation of the acid, seemed strange to them. As this sol was prepared from arsenious oxide with an excess of hydrogen sulfide, the simple explanation is that in their investigation the following exchange was measured:

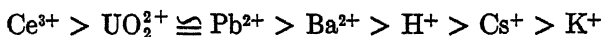


In some cases it had already been observed that an "adsorbed" ion liberated another ion (e.g., Freundlich and Neumann (35)). Michaelis (98) introduced the term "polar adsorption." Mostly, however, exchange of counter-ions was not distinguished from other types of interactions in the double layer, and this often gave rise to strange conclusions and superfluous theories.

A special case of exchange of counter-ions is given by the so-called "base exchange" in permutites, zeolites, clay, etc. However, the amount of

exchangeable ions is here considerably larger. As a consequence of the very peculiar structure of these silicates, studied successfully by F. M. Jaeger (62), W. L. Bragg (14), L. Pauling (101), W. H. Taylor (118), Kelley, Dore, and Brown (66) and others with the aid of x-rays, part of the cations of the *interior* of the crystals are also in free kinetic exchange with a surrounding liquid, and therefore exchangeable by other cations.

Generally the tendency of the ions to substitute another ion diverges considerably. Mostly it is seen that ions of high valence possess a high exchange power. In our silver iodide sols we found the sequence:



The sequence was studied for several types of clay. Jenny (63), among others, found that it varies somewhat with the nature of the clay.

The exchange of counter-ions follows its own rules. First it is clear that there is a natural maximum of the exchange, equal to the amount of available outer ions of the double layer (T). We will assume that both ions stay, independent of each other, in the double layer. Only their average "time of staying" will vary. Then, for two equally charged ions, the following equation may easily be derived (Verwey (128)):

$$T \frac{x_1}{T - x_1} = k \cdot \frac{c_1}{c_2} \quad (3)$$

i.e., the ratio of both ions in the double layer is directly proportional to the ratio in the solution. It is characteristic of the phenomenon that the *ratio* of the concentrations determines the exchange, both ions occurring in the formula being equivalent. If equilibrium is reached, dilution of the system does not cause a shift; the exchange is independent of the dilution.

Exchange isotherms have been measured accurately for permutites only. Most of the experiments were carried out by shaking a sample with a solution containing a cation other than the exchangeable ion of the permutite (say, respectively, 1 and 2). If m grams of the material is used in 1 liter of the solution, c_2 at equilibrium equals the amount mx_1 given back to the solution. (x and T are both given for 1 gram of permutite). Hence, dropping the subscript 1:

$$T \frac{x^2}{T - x} = k \cdot \frac{c}{m} \quad (4)$$

Equations 3 and 4 prove to hold roughly for the exchange for clay and permutites. A similar equation has already been derived empirically by Ganssen (47). Deviations are to be expected, for especially in this case

both ions cannot be considered as acting totally independently. In the crowded cavities and canals of the lattice of these silicates the free energy of an ion will actually differ according to the nature of its neighbors. It is difficult to correct equations 3 and 4 for this effect.⁵ Generally, however, a relation

$$\frac{x_1}{T - x_1} = f\left(\frac{c_1}{c_2}\right) \quad (5)$$

is valid. Most equations used in soil chemistry do not satisfy this condition and therefore do not express the characteristic nature of the exchange of counter-ions (for instance, the equations of Wiegner (139), Wiegner-Jenny (140), Vageler (122), and others). Only the equation of Rothmund and Kornfeld (112), an empirical improvement of that of Ganssen, also satisfies equation 5.

When the exchanging ions differ in valence the relation is more complicated. Jenny found that ions of higher valence substitute other ions relatively stronger when added in small quantities.

Summarizing, we may state that exchange of counter-ions, though a general phenomenon, is but little studied as such, and practically only for artificial and natural soils. It is desirable (from a colloid chemical point of view as well, as will be seen in Part II) to examine this type of "adsorption" with the aid of its proper rules. Not a single concentration, but a ratio of concentrations (or an amount of salt added, c/m) determines the exchange; furthermore, the maximal exchange capacity must be known, i.e., the amount of potential-determining electrolyte taken up, or the total charge of the double layer. That the exchange is not a radical change of the double layer but merely a substitution of its outer ions remains characteristic.

VI. THE ADSORPTION OF ELECTROLYTES

We now consider true adsorption phenomena: the accumulation as a whole of an electrolyte in that part of the solution which is nearest to the surface. Negative adsorption may also occur, viz., when the concentration of the electrolyte added becomes smaller in the boundary layer than in the rest of the solution. According to Gibbs (48) an electrolyte lowers the surface tension when it is positively adsorbed; if it raises the surface tension it is negatively adsorbed. This rule can be easily understood.

⁵ *Note added in proof:* This problem has been attacked by A. H. W. Aten, Jr. (Proc. Acad. Sci. Amsterdam **38**, 441 (1935)) by the simple assumptions that the mutual forces between the adsorbed ions are proportional to x_1 and x_2 and that the distribution is a statistical one. For the present case, this treatment is still a rough approximation.

The surface tension is a measure of the (free) energy which is needed to enlarge the total area of the boundary surface; during this process an adsorption energy is gained when there is a positive adsorption. This adsorption energy lowers the required energy, and therefore the surface tension. From the surface energy we can therefore conclude immediately as to the sign of the adsorption. Thus it can be proved that from aqueous solutions most electrolytes are negatively adsorbed at the surface.

We have stated several times that the "adsorption" phenomena described in the previous sections are not adsorptions in the proper sense. This will be clear at once in the case of the exchange of counter-ions. But neither does assimilation of potential-determining electrolytes satisfy Gibbs' definition of adsorption. The difference is that one ion of the potential-determining electrolyte goes from the solution into the other phase, causing there a surface charge, which theoretically might also be effected from within this phase by means of an external electric current. Thus the surface tension is no longer connected directly with the accumulation of electrolyte in the boundary layer, but only indirectly as a consequence of the charge of the double layer thus formed. A real adsorption from a solution is *not* accompanied by a change of the *total* boundary potential drop. Therefore in the case of the "adsorption" of potential-determining electrolytes the surface energy also contains an electrical energy.

Nevertheless, if real adsorption occurs, the situation in the double layer may be seriously complicated. Important conclusions may be deduced from investigations in which the properties of the double layer are examined for the somewhat unusual adsorbents air and mercury.

Generally speaking, an ion in the boundary layer is subjected to two groups of forces: the attraction by the surface and that by the water molecules (hydration). If, for both ions, the latter is stronger, the adsorption will be negative.

It is clear that this case will be realized with the system air-solution. On account of their thermal movement some ions will get into the boundary layer, but the stronger their hydration, the more strongly they will be forced back into the bulk of the liquid. Cations are generally more strongly hydrated than anions; hence the cations especially are held back in the solution, and the ions that reach the boundary will be mainly anions. This means a separation of charges; the boundary layer is charged negatively with respect to the liquid layers further inside. In the outer layers of the solutions there is, therefore, a potential drop, caused by a spontaneous orientation of the (negatively adsorbed) electrolyte. This potential drop has been measured by Frumkin (43) for a large number of electrolytes. For 2 *N* solutions the values found were (in millivolts):

potassium thiocyanate, -87 ; ammonium thiocyanate, -87 ; barium thiocyanate, -87 ; sodium iodide, -55 ; potassium iodide, -52 ; potassium bromide, -16 ; potassium chloride, -6 . It is actually seen that the cations penetrate only slightly into the double layer, for their influence upon the potential drop is negligible. Furthermore there is a distinct "lyotropic" sequence for the anions. Of all ions the thiocyanate ion gives the largest potential, or penetrates into the boundary layer most easily; it lowers the surface tension least, or gives the smallest negative adsorption. It has actually the largest radius, or the lowest hydration.

In the case of mercury-solution the forces from the surface are generally stronger than the hydrating forces. One of the reasons is that the ions induce in the mercury phase a charge of the opposite sign which favors the attraction; this additional force can be calculated by considering it to be due to an opposite charge in the metal, which is the image of the

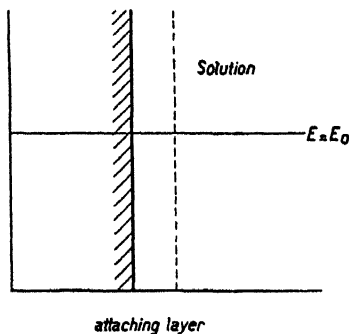


FIG. 5. Potential curve in the zero point of the charge

charge of the ion ("Bildkraft"). Specific forces also play a part. We see, therefore, that most electrolytes are adsorbed positively; a few electrolytes with strongly hydrated anions (arsenates, phosphates, carbonates) raise the surface tension slightly. The potential drop caused by these adsorptions cannot be measured directly in this case, since the total potential drop is only sensitive to the concentration of the mercury ions in the solution. Though the total potential drop of the double layer is therefore not altered by adsorption of an indifferent electrolyte, the potential slope within the double layer may be changed thoroughly by it. We shall have to consider this more in detail.

Suppose we have a surface, e.g., of mercury, in contact with an aqueous solution, and bring on such a potential that the surface is uncharged ($E = E_0$). We now dissolve some potassium iodide in the solution. This electrolyte is adsorbed positively; it accumulates in the boundary layer in such a way that the iodide ions approach the surface more than the

potassium ions. In other words, mainly iodide ions get into the "attaching" layer of Stern. This orientation gives rise to the potential drop mentioned above, localized in the outer part of the double layer. As the total potential drop is kept constant, this local potential drop must be compensated somewhere else. This occurs through a precipitation of mercury ions upon the surface (or a dissolution of electrons), charging the mercury positively. The situation before and after the addition of potassium iodide is represented by figures 5, 6a, and 6b. The slope of the potential as a function of the distance is also indicated qualitatively. Since for our reasoning only that part of E which is due to free charges is important (i.e., the part $E - E_0$), in these figures it is assumed for convenience that $E_0 = 0$. Furthermore we give in figure 6a a situation which is valid only for a non-conducting surface (dielectric); in the case of mercury, however, each ion induces its image (of the opposite sign) in the

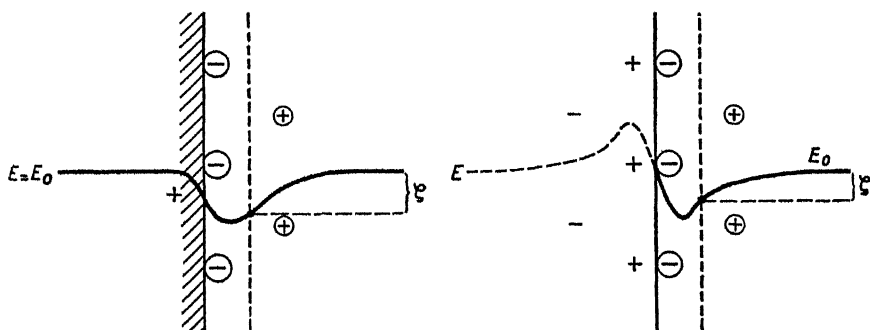


FIG. 6. Potential curve for the adsorption of anions on a previously uncharged surface (a dielectric and a metal respectively).

metal, and this leads to figure 6b. The potential in the outer layer is not influenced fundamentally by these image powers. The counter-ions are distributed over the "attaching" and the "diffuse" layer; this detail is omitted in the figures in order to avoid complications.

In the case of figure 5 not only E (or $E - E_0$) is zero, but also $\zeta = 0$. After the addition of potassium iodide, however, ζ will be negative, though the mercury is charged positively, and $E - E_0$ is still zero.

If now E is made more positive, the positive charge of the mercury, but also the adsorption of iodide ion, increases. The result is given by figure 7 (a and b).

If, however, we wish to reach the new zero point of the charge, we must give to E a more negative value. This is shown in figure 8.

Thus we see that upon the adsorption of an indifferent electrolyte a shift of the zero point of the charge occurs, mostly to more negative values

of E . This shift, and therefore the adsorption, can be measured with the aid of the electrocapillary curve, which represents the surface tension as a function of E . As the surface tension is lowered by a surface charge (the energy necessary for the enlarging of the surface is then partly delivered by the mutual repulsion of the surface charges), the curve has a maximum for $E = E_0$. Gouy (49) and later Frumkin (45) measured the electrocapillary curve of mercury in solutions of several electrolytes. They found for 1 N solutions a shift of the maximum: for potassium sulfide, -420

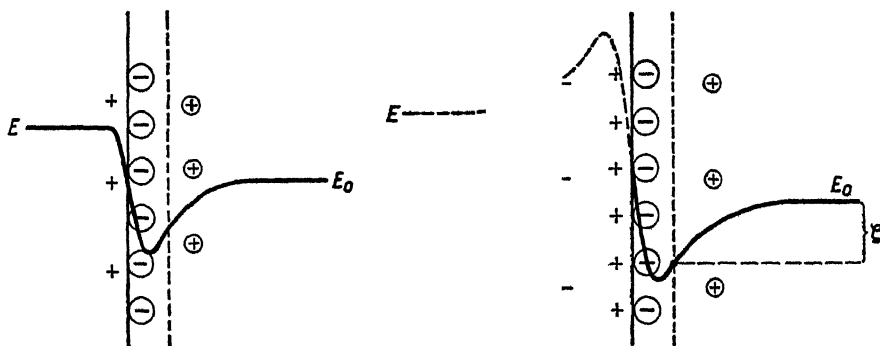


FIG. 7. Potential curve for the adsorption of anions on a positive surface

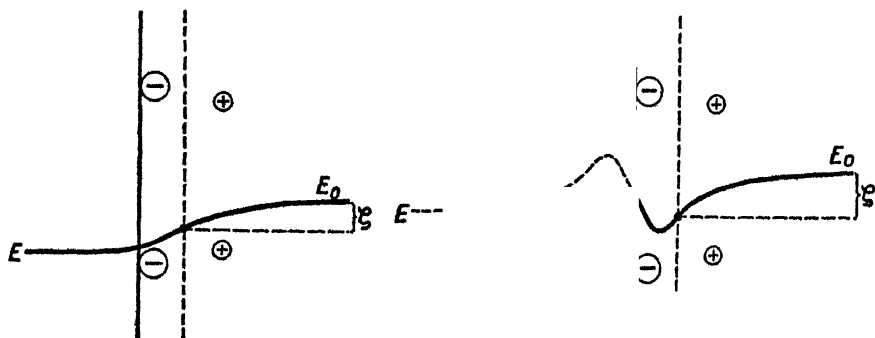


FIG. 8. Potential curve for the adsorption of anions; shifted zero point of the charge.

millivolts; for potassium iodide, -320 millivolts; for potassium thiocyanate, -220 millivolts; for potassium bromide, -150 millivolts; for potassium chloride, -60 millivolts. In $0.1 N$ potassium iodide it is -220 , in $0.01 N$ potassium iodide -160 millivolts. Hence the orientation of the adsorbed ions is stronger than at the surface of air, but again the anions are adsorbed primarily. Also we see that the larger or less hydrated anions are adsorbed more strongly, but the sequence is not exactly the same; this is in accordance with the already observed fact that not only

hydrating forces (which determine the lyotropic series) but also the attraction by the mercury govern the adsorption. Hence several other factors play a part, such as polarizability of the ions, eventually the dipole moment and the place of the latter in the molecule, and van der Waals forces (cf. van Arkel and de Boer (5)).

Figure 9 gives a number of electrocapillary curves. In the case of adsorption not only does the maximum shift to more negative values of E ,

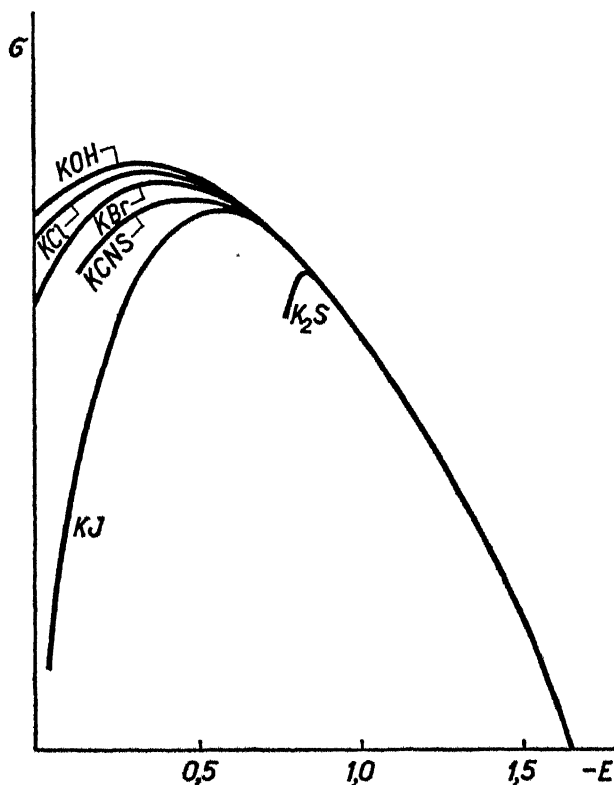


FIG. 9. Electrocapillary curves of various electrolytes (σ = surface tension mercury-solution; E = potential of the mercury).

but the surface tension is also lowered; for a mercury surface that is charged strongly negatively all curves coincide, i.e., the adsorption of the anion is reduced to zero.

From the investigations of Gouy and Frumkin we may conclude that the adsorption of indifferent electrolytes is a rather complicated process. The fact that it is always accompanied by a disturbance of the equilibrium of the distribution of potential-determining electrolytes has often been

overlooked. Inversely, the charge of the surface has a great influence upon the magnitude of the adsorption.

We cannot illustrate these conclusions with direct measurements of the adsorption, since only a small number of reliable investigations of this kind exist. This may seem strange, since a large number of measurements are found in chemical literature. Sometimes, however, these measurements are not very accurate, or they have been carried out with inadequately defined substances. Often they are concerned with true adsorption only in part or perhaps not at all (sections IV, V, and VII). Horovitz and Paneth (59), Fajans (31), Hahn (53), Imre (61) and others tried to give exact "adsorption rules" or "adsorption laws," but their theoretical considerations cannot be accepted, since they do not sufficiently take into account the principles given in these sections, or do not distinguish different phenomena in their interpretation of experimental facts.

Some valuable conclusions can be drawn from an investigation of Miss de Brouckère (15), in which a (positive) adsorption of several electrolytes by barium sulfate was measured with much care. It was affirmed for many cases that the anion and the cation were adsorbed in equivalent amounts. In dilute solutions she found that $\log x$ varies linearly with $\log c$ (x = amount adsorbed, c = concentration of the electrolyte when equilibrium is reached), i.e., Freundlich's isotherm seems to hold good for the adsorption of electrolytes. Again the anion leads the adsorption and for the halides the sequence $I^- > Br^- > Cl^-$ exists.

In the laboratory of Kruyt the adsorption of electrolytes was studied by Janssen (64), using another indirect method. Accurate measurements of the streaming potentials of glass capillaries filled with different electrolytes of varying concentrations were carried out. From the ζ - c curves thus obtained Janssen calculated the corresponding charges of the diffuse layer with the aid of Gouy's theory. Thus he found that this electrophoretic charge increases strongly upon the addition of bromides, chlorides, etc. Janssen assumes that this charge is directly proportional to the amount of anions adsorbed; this is not quite correct, for it neglects the shift of the equilibrium of the potential-determining ions discussed in this section, but in the present case it may be useful as a first approximation. From his data and from earlier experiments of Kruyt and van der Willigen (78), he finds that again in dilute solutions the adsorption obeys the equation

$$d \log x = k \cdot d \log c$$

For higher concentrations saturation occurs (apparent radius of the ions about 10^{-7} cm.). Similar calculations with about the same result have been published by Abramson and Müller (1) and by Mooney (93). Janssen

has tried to give a theoretical foundation for his results. Starting from Langmuir's well-known adsorption isotherm for neutral molecules he derives the electrical factor which must be added in order to make the equation applicable to the adsorption of electrolytes. Janssen concludes that actually Freundlich's isotherm must hold approximately for this case, and calculates for the constant k_2

$$x = k_1 c^{k_2} \quad (6)$$

the value $2/3$. The last conclusion is affirmed by his experiments.

Summarizing, we may state that we have found another characteristic in which the adsorption of indifferent electrolytes differs from the "adsorption" of potential-determining electrolytes; for the latter $dx = k \cdot d \log c$, while for the former $d \log x = k \cdot d \log c$.

VII. EXCHANGE OF LATTICE IONS

Recent investigations of Kolthoff and his coworkers proved that sometimes a lattice ion can also be replaced by ions added to the solution. Kolthoff suggests that many cases of "adsorption" are actually exchanges of this type, as for instance, in the well-known "adsorption indicators" of Fajans-Kolthoff for the titration of silver halides, etc. We need make only a few remarks about this fourth type of "adsorption," since Kolthoff's work on this subject has not been finished and its significance for our theme is not yet clear.⁶

An exchange of lattice ions by an electrolyte solution in contact with the crystals was first stated by Kolthoff and Rosenblum (70); upon the addition of the sodium salt of Ponceau 4R to a suspension of lead sulfate, the dye anions substitute the sulfate ions of the lattice surface. Kolthoff, Rosenblum, von Fischer, and Sandell (71, 73) found several other cases of this exchange "adsorption," including some inorganic ions. A similar exchange has already been observed by de Boer (8) in his experiments on the adsorption of vapor molecules by a salt layer. Alizarin vapor, $C_6H_4(CO)_2C_6H_2(OH)_2$, is adsorbed in a monomolecular layer by calcium fluoride (see section III). Upon heating the adsorbed layer acts chemically with the fluoride ions of the salt, and hydrogen fluoride is liberated. Thus the alizarin ions substitute two fluoride ions of the lattice. At the same time the adsorbed layer changes its color.

To some extent the same principles hold for this exchange as were

⁶ *Note added in proof:* In a paper appearing before long in the *Kolloid Zeitschrift*, the author has shown recently that this "exchange of lattice ions" is probably not a new type of "adsorption" but might be interpreted as a combination of the phenomena of the preceding sections, effected by a strong adsorbability of one of the ions added.

derived in section V for the exchange of counter-ions. The difference, however, is that one of the ions here is a potential-determining ion. Both ions are therefore not equivalent. On account of the exchange the total potential drop is changed; in the case of the experiments of Kolthoff and Rosenblum, sulfate ion is replaced in the surface, and the concentration of these ions in the solution will thus be increased. The charge of the lead sulfate becomes more negative, and this certainly has some influence upon the exchange.

In all the experiments of Kolthoff the solubility product of the newly formed compound was not reached. It seems therefore as if its "solubility" in a monomolecular layer upon a lattice already present is lower than its solubility as a separate phase. We may therefore describe the phenomenon as a two-dimensional precipitation.

VIII. SUMMARY

We have examined the structure and the origin of the electrical double layer. The influence of added electrolytes was studied. As a whole we met four fundamentally different phenomena generally denoted by the name of adsorption. Only one of them is an adsorption in the proper sense, and it seems desirable to distinguish the others with the aid of more characteristic names, viz., assimilation of potential-determining electrolytes, exchange of counter-ions, and exchange of lattice ions.

In Part II we shall examine the significance of our foregoing considerations for the problems of lyophobic colloid chemistry.

II. THE STABILITY OF LYOPHOBIC COLLOIDS

I. INTRODUCTION

A lyophobic sol can lose its stability in two different ways: (1) by coagulation or (2) by coarsening. Coagulation is the formation of larger agglomerates or "polyons" (Zsigmondy), in which the particles have maintained their individuality. Thus coagulation means that the regular distribution of the particles through the dispersion medium is disturbed without decrease in the degree of dispersion. For this process the ζ -potential is of the utmost importance. Coarsening is a decrease in the degree of dispersion. During this process the smaller particles go into solution and the larger particles grow continually. Coagulation usually occurs in less than a second, whereas coarsening is rather slow. Coarsening will occur if the energy which is gained by a decrease of the total boundary surface (determined by the surface tension) is larger than the electrical energy of the double layer; for this process the total potential drop of the double layer is determinative.

Several authors have tried to calculate the colloidal equilibrium, deter-

mined by the concurrence of electrical and surface energies. Rather complicated and not always correct calculations have been published by Gyemant (52), O. K. Rice (111), March (92), and W. C. M. Lewis (89). It is remarkable to see that each one of them, obviously ignorant of the work of the others, made the same mistake. All of them thought that they calculated the stability with regard to coagulation and used ζ as a physical constant; actually they calculated the stability in the sense of coarsening and tried to determine the degree of dispersion as a function of the properties of the system.

Proof that such calculations must fail is that the condition of equilibrium which is sought does not exist. Colloid chemical experience reveals that a lyophobic sol is never stable in the sense of coarsening and that coarsening always occurs, though in some cases only very slowly. This means, as Kruly (74) especially has emphasized repeatedly, that *a colloidal system is never a stable system in the thermodynamic sense*. There is no definite degree of dispersion which is more stable than others; the degree of dispersion of a sol depends solely on its method of preparation and further treatment. Obviously the electrical energy of the double layer is not sufficient to stabilize a sol in the sense of coarsening; the most stable state has the smallest total boundary surface, i.e., is coarsely crystalline.

This coarsening process occurs with a velocity that depends largely on the solubility of the disperse phase; apart from this factor it is accelerated, like every other diffusion process, by the elevation of the temperature. Thus the negative sols of silver chloride, silver bromide, and silver iodide, peptized with small quantities of halide, differ strongly in their tenability. Silver chloride, with a comparatively large solubility (in pure water about 10^{-5} equivalent per liter), gives sols which are destroyed in a few days by coarsening. Silver iodide sols, however (solubility 10^{-8}), are tenable during several years. The "stability" of sols of silver bromide and the solubility of silver bromide are intermediate between those two extremes. The coarsening of silver bromide is well known in the process of "ripening" of the photographic "emulsion."

Upon the addition of potassium iodide the solubility of silver iodide increases greatly. According to Hellwig (55) the solubility of silver iodide in 0.33 *N* potassium iodide is 0.4×10^{-3} equivalent per liter. Therefore the rate of coarsening increases enormously if potassium iodide is added to the sols (Verwey and Kruly (124)); elevation of the temperature has the same effect.

Coagulation and coarsening of sols are often confused; this may give rise to totally wrong conclusions or theories. This was the case, for instance, in recent work of Basinski (60) and von Weimarn (132). Also Imre's (61) "coagulating precipitates" are rapidly coarsening sols.

Although, strictly speaking, a lyophobic sol is never "stable," we nevertheless speak of the "stability" of a sol in terms of its stability toward coagulation (in sense 1). The problem of the stability of lyophobic colloids is therefore of quite another nature than was supposed by Gyemant, Rice, and March. An exact theoretical treatment of this problem requires an estimation of the forces of cohesion and of the forces that prevent cohesion. These mutual attractive forces can be said to act over a distance of only a few molecular dimensions; this we learned, for instance, from the kinetics of flocculation, for which a very valuable theory was developed by von Smoluchowski (115). In this theory it is assumed that the attractive forces are practically active only at the moment when the particles collide; this seems a very good approximation of the real state of affairs. Presumably the attractive forces between the particles are therefore due to the van der Waals forces between the atoms or ions in the surface of the particles. They are thus of the same type as the forces that keep the molecules of a non-polar liquid close together. This type of attraction between two atoms drops rapidly with the increase of the distance ($\sim \frac{1}{r^6}$).

Generally the particles will have such an irregular habit that, in the flocculated state, they touch each other only in a few superficial lattice points. Actually, there seems to be only a very loose bond between the particles, for several colloids can easily be peptized again, at least immediately after coagulation. If the flocculated sol is allowed to stand for a longer time, the contact between the particles becomes more intimate. In connection with this, typical aging phenomena (rapidly decreasing adsorbent properties, recrystallization, etc.) are observed with many flaky precipitates (cf., e.g., Freundlich and Haase (37) or Kolthoff (69)). But it is clear that the coarsening process will be accelerated considerably in such flocculated agglomerates; crystal faces can grow together or can be cemented together by molecules (ions) diffusing through the solution and coming from other parts of the crystals. These are all secondary processes in the coagulated state and have no influence upon the flocculation itself, which seems to be a reversible process (cf. also Kruyt and van Arkel (76) or Burton and May Annetts (18)).

Although we do not know exactly which points of the surface will tend preferably to adhere to similar surface spots of other particles, it seems possible, from the considerations mentioned above, to give a rough calculation of the magnitude of the mutual attractive forces between the particles of a given sol. It is much more difficult to give a quantitative computation of the repulsive forces which prevent them from sticking together. We know that these repulsive forces are of an electrical nature. We have seen in Part I that, if a double layer is present, the particles are

surrounded by a partly diffuse outer charge. If a particle in its Brownian movement approaches another one, their ionic spheres will penetrate into each other, and from this a repulsion results when there is still a discrete distance between the particles. An exact calculation of this repulsion as a function of the properties of the double layer has never been given.⁷ For the present, we will use the *empirical* fact that a certain "critical" value of the ζ -potential is needed for stability (Powis (103), Kruyt and Briggs (79)), i.e., that a definite potential drop in the diffuse outer layer is required in order to keep the particles far enough from their mutual attraction fields. If we start from the empirical point of view that the stability is connected intimately with the magnitude of the ζ -potential of the particles, the problem remains, in what way this ζ -potential depends on the structure of the double layer, the nature and the concentration of electrolytes present, etc. It is this problem that we shall have to examine first in the following sections.

II. PRIMARY STABILITY

Accepting the "stability" of a sol in the restricted sense discussed above, we can still distinguish two types: (1) A sol acquires its *primary stability* by the formation of a double layer which has a sufficiently high ζ -potential. This phenomenon is generally called "peptization." (2) The stability of a sol once formed is affected by addition of foreign electrolytes. This is a question of *secondary stability*.

Several concepts of peptization exist. Sometimes it is believed that the small amount of electrolyte required for the peptization acts chemically with the surface of the particles. Thus the SnO_3^{--} ion is assumed to be at the inside of the double layer of SnO_2 sol, peptized with potassium hydroxide (Zsigmondy). The ferric oxide sol is often thought to be charged positively by the dissociation of FeOCl into FeO^+ and Cl^- . Pauli generally assumes the formation of complex ions of the Werner type in the surface of the particles. Other investigators believe peptization to be a consequence of a "specific" adsorbability of certain ions (Perrin, Freundlich).

A valuable contribution to the problem of peptization was given by the well-known work of Lottermoser (91), who stated (1907) for the first time that the stability of positive and negative silver iodide sols is governed by the "adsorption" of the proper ions of the precipitate (cf. also Fajans and von Beckerath (31)).

⁷ Note added in proof: A very interesting attempt in this direction has been made recently by Levine (Proc. Roy. Soc. London **146**, 597 (1934)), in calculating the sedimentation equilibrium in colloidal suspensions.

However, all these different interpretations, though essentially correct, are restricted to special types of sols and have no general validity for all cases.

A more precise conception was given by Kruyt and van der Willigen (80), who tried to extend earlier considerations of Fajans and Mukherjee. They observed that the ζ -potential of different substances can be increased by all kinds of electrolytes (cf. also Mukherjee (94, 95)); but only those ions which "fit" into the lattice of the particles can peptize the substance. Thus silver iodide can be peptized by small amounts of I^- , Br^- , Cl^- , CN^- , SCN^- , but not by NO_3^- , CO_3^{--} , PO_4^{--} , or $Cr_2O_7^{--}$. If certain precautions are taken it can be shown that hydroxide ion also is unable to stabilize a negative silver iodide sol (Verwey and Kruyt (124)).

This rule of Kruyt and van der Willigen has been confirmed for several other sols by Cysouw (25), e.g., for insoluble sulfides, selenides, complex cyanides, etc. Those ions which form isomorphous crystals with the substance to be peptized were always able to give more or less stable sols. A few exceptions, however, were found, e.g., the complex cyanides were peptized by cyanide ion (Kruyt and Cysouw (80a)).

On the basis of our considerations in Part I it is easy to give a full explanation of these regularities and, at the same time, a better formulation of the apparent exceptions. We have stressed the fact that there is a fundamental difference between the building up of the double layer by means of the assimilation of potential-determining electrolytes and the formation of a double layer on account of pure adsorption phenomena. In the latter case there is only an orientation of ions in the solution nearest to the surface, not a separation of charges over two phases. It seems therefore plausible that the building up of a first double layer is required for primary stability. Thus *only potential-determining electrolytes will be able to peptize a substance*. This law actually includes the rule of Kruyt and van der Willigen, since, as we have seen in Part I, section III, all ions that both phases have in common are to be considered as potential-determining ions, and are subjected to an equilibrium of distribution over both phases which causes the formation of the double layer.

The essential fact that only potential-determining ions and not indifferent electrolytes cause primary stability is undoubtedly connected with the fundamentally different behavior with regard to their concentration. The ζ -potential is raised by an increase of the free charge of the double layer (charge η_2 ; see Part I, section III), but it is lowered by an increase of the concentration of electrolytes in the solution (cf. Part II, section III). If now an increase of the charge is caused by the addition of an electrolyte, it is seen that there are two counteracting tendencies. Those electrolytes will give a high potential to the double layer that are "ad-

sorbed" relatively strongly for the smallest concentrations. The conditions are much more favorable for potential-determining electrolytes; in this case $dx = k \cdot d \log c$ holds; for pure adsorption, however, $d \log x = k' \cdot d \log c$. We can compare, for example, the "adsorption" of potassium iodide by 1 m.² silver iodide (calculated from our measurements on dialyzed silver iodide sols (126), interpolated, and extrapolated to the zero point of the charge $c_{I^-} = 10^{-10}$) and the adsorption of potassium iodide by 1 m.² barium sulfate (calculated from the measurements of Miss de Brouckère (15)):

c	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}	10^{-9}	10^{-10}
$x(\text{AgI})$		0.56	0.48	0.40	0.32	0.24	0.16	0.08	0.00
$x(\text{BaSO}_4)$	0.77	0.25	0.056	0.009					

It is seen that both "adsorptions" occur in quite different concentration regions. The potential-determining electrolyte goes into the double layer when the concentration in the solution is still extremely small, and its lowering influence upon ζ negligible. The indifferent electrolyte, however, is adsorbed to the same extent at very much higher concentrations, where the lowering of the potential is considerable.

The advantage of our conception of primary stability is that it enables a more quantitative treatment of these problems. In a given case the primary stability of a sol is determined wholly by a few physically well-defined magnitudes: *the concentration of its potential-determining ions and the situation of the zero point of the charge*. The author (127) calculated for dialyzed silver iodide sols a total potential drop due to free charges ($E - E_0$) of about -0.2 volt. We have seen in Part I, section III, that the ζ -potential is only a fraction of this (about one-third), since part of the potential drop occurs in the silver iodide phase and in the "attaching layer" (cf. figure 2). The "critical" value of $E - E_0$, required for primary stability, will thus be almost three times the critical ζ . Usually a value of ± 40 millivolts is given for the latter. From this a critical $E - E_0$ of about 120 millivolts should be expected (for dialyzed silver iodide sol). This agrees very well with the experimental facts, for it is found that a value of $E - E_0$ of about 2×0.058 millivolts is required for stability. A positive silver iodide sol flocculates when its concentration of free silver ions is lowered to about 10^{-4} (e.g., by dialysis); the zero point of the charge is reached at $c_{\text{Ag}^+} = 10^{-6}$; a dialyzed negative silver iodide sol ($c_{\text{Ag}^+} = \text{about } 10^{-9}$) is stable, but flocculates when its c_{Ag^+} is raised (e.g., by careful titration with very dilute silver nitrate solution) to about 10^{-8} .

If there is sufficient knowledge of the structure and properties of the double layer for a given sol, theoretically it should be possible to predict its primary stability conditions, provided that its particles are large enough

for the approximative use of the theory of the flat double layer. At present, however, our knowledge is inadequate. Moreover, we do not even know the situation of the zero point of the charge for most of the sols.

For the present a more qualitative survey will therefore be given, in order to show that our concept may be very useful for the interpretation of peptization. In any event it is superior to "chemical" or other interpretations.

It is clear that our concept can be easily extended to all colloidal salts. For this case it is very simple to indicate what ions build up the double layer and thus determine the potential drop in it. For instance, in an arsenic trisulfide sol, prepared with the aid of hydrogen sulfide as a peptizer, the concentration of the free sulfide ion in the sol determines the charge and the potential of the double layer. The older concepts of peptization were developed mainly for sols of other types, especially the sols of hydrous oxides (Fe_2O_3 , Cr_2O_3 , Al_2O_3 , ThO_2 , SnO_2 , SiO_2), of silicates (glass, clay, permutite), the noble metals, or carbon. In all these cases hydrogen ion and hydroxide ion have to be considered as potential-determining ions. The particles of the latter sols either contain water in the bound state, or dissolve hydrogen and oxygen and may thus function as gas electrode. In all these cases the charge and the potential of the double layer are governed by the pH of the sol medium. Inversely, we may state that only these substances can be peptized by hydrogen ion or hydroxide ion. This is the essential explanation why a silicate is peptized by potassium hydroxide and silver iodide is not.

Obviously the important rôle of hydrogen and hydroxide ions in soil and colloid chemistry is connected with the circumstance that they are frequently potential-determining ions. The situation of the zero point of the charge seems to be a highly interesting problem for such sols as Fe_2O_3 , Al_2O_3 , and Cr_2O_3 , since they can exist in both the positive and negative state. Thus a logical distinction between "acidoids" and "basoids" (Michaelis⁸) can be drawn, according to the situation of the zero point of the charge related to $\text{pH} = 7$. It is remarkable that the positive sols of the hydrous oxides just mentioned show exactly the same reversion of the charge upon their dilution (Lottermoser and Riedel (91a)) as was stated earlier by Kruyt and van der Willigen (80) for the positive silver iodide sol. These reversions are a consequence of the decrease of the concentration of the potential-determining ions (hydrogen ion, silver ion) by the dilution.

The chemical concept has been accepted especially by Zsigmondy and

⁸ Also the isoelectric point (Michaelis (87)) of albumin and other lyophilic colloids is quite analogous to the zero point of the charge of our lyophobic sols.

his collaborators (142), for instance in their excellent investigation of the SnO_2 sol. Zsigmondy, however, is apparently well aware of the fact that the chemical terminology is merely a useful method for the description of physical phenomena. Indeed, modern concepts of the structure of molecules (van Arkel and de Boer) illustrate that the discrepancy between chemical and physical theories of the phenomena is quite imaginary. Whether the negative charge of a hydrated stannic oxide particle is due to the formation of SnO_3^{--} ions in the surface or is caused by the "adsorption" of hydroxide ion is fundamentally indistinguishable. In certain cases the chemical formulations may be handy and advantageous, as in the work of Zsigmondy, Franz, and Heinz (142); we have to keep in mind, however, that the SnO_2 sol, as to its secondary stability, forms an exceptional case (see section V). For most other sols the advantages of a chemical formulation of the phenomena are much less obvious. Our concept is therefore the more general one, and moreover enables a quantitative treatment.

Another field where chemical descriptions of the phenomena may be substituted successfully by a more exact theory is that of the organic sols with acid or basic groups in the molecule (mastic, gamboge, congorubin, etc.). Also the *electric* stabilization factor of most lyophilic colloids must be governed by regularities similar to those for the primary stability of silver iodide sol. We cannot deal with these problems here in detail, but investigations of Tartar (119, 120), Michaelis (96), Janet Daniel (26), and others yield very interesting support of our views and show clearly the important rôle of the potential-determining hydrogen ions for the primary stability of these organic sols (cf. ref. 130).

Finally it seems superfluous to point out that the assumption of a "specific adsorbability" of certain ions in order to explain peptization can be dealt with in the same way. The assumption, indeed, as it stands, is a very inexact formulation, since (as we have seen in Part I) several different phenomena are generally included by the term "adsorption." Unsatisfactory, too, is the use of Coehn's rule to explain the origin of the charge (23, 24) (see, for instance, ref. 104).

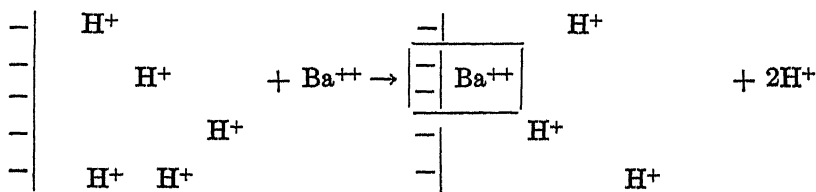
Summarizing, we state that primary stability (peptization) is governed by the distribution equilibrium of the potential-determining ions which are responsible for the formation of the electrical double layer. Peptizing ions are potential-determining ions. The primary stability of a sol is thus connected intimately with and might be calculated from the concentration of the free potential-determining ions in the solution and the situation of the zero point of the charge. The significance of hydrogen ion and hydroxide ion as potential-determining ions has been discussed for many sols.

III. SECONDARY STABILITY; THEORIES OF FREUNDLICH AND MÜLLER

We have seen that by the "secondary stability" of a sol is meant its stability once the double layer is formed, with regard to indifferent electrolytes added to it. Schulze (113) and others studied the flocculating values of different electrolytes for several sols. It is well known that characteristic differences between different electrolytes are found if the valence of the ion that is charged oppositely to the colloidal particles is varied. For the flocculation of a negative sol the following is required: 25 to 100 milliequivalents per liter of a 1-1, 1-2, 1-3, etc., valent electrolyte; a few milliequivalents of a 2-1, 2-2, 2-3, etc., valent electrolyte; 0.1 to 1 milliequivalent of a 3-1, 3-2, etc., valent electrolyte. The flocculating values of different cations of the same valence generally do not differ much, and the differences for electrolytes with varying anions are of the same order. The rule of Schulze-Hardy, it is true, has a number of exceptions.

It seemed that both the rule and its exceptions could be explained conclusively by Freundlich's flocculation theory (33, 34). Freundlich and Gann (38) have summarized this theory into four theses. The first two can be formulated as follows: (1) In order to coagulate a sol the particles must be neutralized to a definite point, i.e., a definite amount of the charge must be removed. (The remaining charge, just sufficient to prevent coagulation, is then the "critical" charge.) (2) The neutralization of the particles occurs by the adsorption of oppositely charged ions.

Let us consider a particle of As_2S_3 , peptized by hydrogen sulfide. A small amount of barium chloride is added to the sol. According to Freundlich the barium ions are adsorbed, decreasing the charge of the particle:



A number of hydrogen ions, corresponding to the decrease of the charge ($5 - 3 = 2$), are given back to the solution.

It has already been stated by Freundlich and Neumann (35) that the number of hydrogen ions set free is actually equivalent to the amount of cation "adsorbed." They used organic cations (morphine, new fuchsin) as the "flocculating ions." This equivalence was affirmed by several investigators (Rabinowitch (116) and Weiser (133, 135)) for other sols and electrolytes. Occasionally, it is true, a "supraequivalent" substitu-

tion was believed to occur (Rabinowitch (106, 107)), but Weiser (133, 134) proved the incorrectness of these experiments. Other deviations will be discussed below.

Hence according to Freundlich's theory the "flocculating ions" and the ions already present in the double layer have a different function. The ions penetrating into the double layer are "adsorbed" at the same time, i.e., they go into the immobile part of the outer layer, decreasing the free charge of the particles. Another picture of the "neutralization" of the particles seems impossible. It is clear, however, that a variation of the *total* charge cannot be the general cause of this neutralization; the total charge can change greatly only when the concentration of the potential-determining ions is changed (eventual complications on account of pure adsorption, to be discussed later, will be neglected for the present). Thus the "neutralization" of Freundlich's theory must be considered as a shift from free to immobile charge, an increase of η_1 and a corresponding decrease of η_2 (Part I, section II).

The *second* supposition can be tested comparatively easily. Suppose that we flocculate a sol with different electrolytes, adding a just sufficient amount of each; the charge of the particles must then be decreased by the same constant amount, i.e., the particles have "adsorbed" equivalent amounts of the different oppositely charged ions. We shall see that this test has been applied several times.

In order to give a more detailed explanation of the regularities observed in the flocculation of lyophobic colloids, two other suppositions were added to the former: (3) For the adsorption which effects the neutralization of the particles the usual isotherm is valid. ($x = k \cdot c^p$; k and p are constants, $p < 1$). (4) Calculated in moles the isotherms of different electrolytes coincide, with the exception, however, of a few strongly adsorbable (mostly organic) ions.

With the aid of these suppositions Freundlich was able to give his well-known explanation of the rule of Schulze-Hardy. If we compare, for example, for a negative sol the action of electrolytes with a mono-, di-, and tri-valent cation, their isotherms will be represented, according to supposition 4, by one single curve (figure 10). According to suppositions 1 and 2, the amounts adsorbed in order to reach flocculation should have the ratio 1:1/2:1/3 (for mono-, di-, and tri-valent cations, respectively) expressed in moles. In figure 10 these amounts are given by a, b, and c. The corresponding concentrations (if the sol is not too concentrated these will equal the flocculating values) must be in the ratio $c_I:c_{II}:c_{III}$. It is seen that, as a consequence of the typical form of the adsorption isotherm, there are actually large differences between the flocculating values of the electrolytes considered.

For a strongly adsorbable cation the isotherm will have a deviating form (curve B), and the flocculating value will thus be abnormally low (for a monovalent ion, e.g., c_1').

Freundlich has tried to prove this theory in different ways. The second, third, and fourth suppositions were subjected to various experimental tests. Suppositions 3 and 4 have been studied mainly in older investigations (34), which do not seem to be very accurate or convincing. The second supposition, however, the equivalence of the amounts adsorbed at the flocculation concentration, seemed to be confirmed by experiments

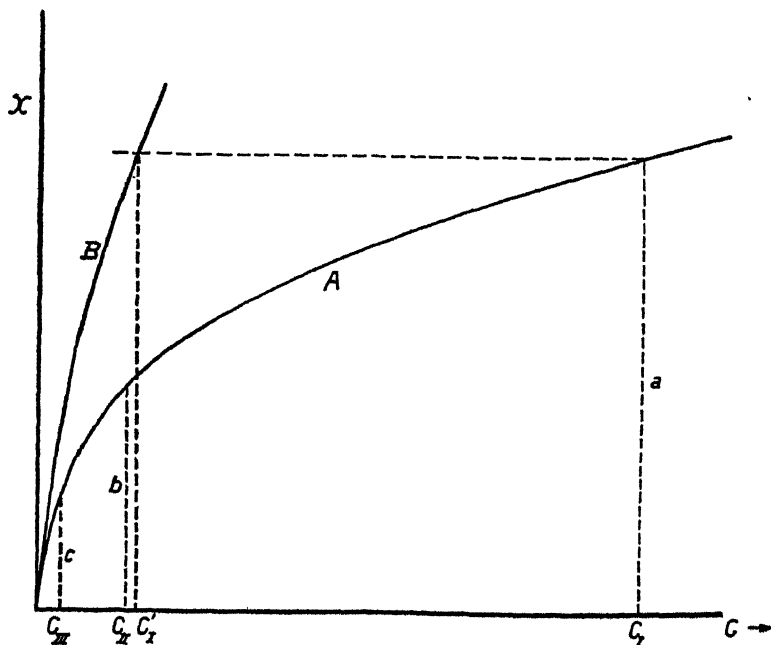


FIG. 10. Explanation of Schulze-Hardy's rule in the old Freundlich theory

with As_2S_3 sol, HgS sol (Freundlich and Schucht (36)), Al_2O_3 sol (Freundlich and Gann (38)), etc. In all these cases more or less equivalent amounts of the oppositely charged ions were carried down by the coagulating particles. For a long time Freundlich's theory was therefore accepted by various colloid chemists.

Several other investigators gathered experimental data, e.g., for Fe_2O_3 sol, which seemed to contradict Freundlich's conceptions. A survey of the discussion on this point is given by Weiser (136) in Alexander's *Colloid Chemistry*. We will not follow it in detail, as Freundlich finally settled it in 1929, admitting the untenability of his theory. Freundlich, Joachim-

son, and Ettisch (41) again measured the "adsorptions" of a large number of cations at the flocculation point of an arsenic trisulfide and a gold sol. This investigation revealed that actually the amounts of cation carried down by the flocculating particles were mostly *not* equivalent. The differences are so considerable, indeed, that Freundlich's negative conclusion seems justified, though there may be some doubt with regard to the analytical accuracy of part of the measurements. In some cases, for instance, the changes of the concentrations of both anions and cations were determined; from these data it seems that the electroneutrality was disturbed, which is obviously impossible. Moreover, Rabinowitch (110) has tried to check Freundlich's investigations, and has stated that the latter's methods were not quite correct. He therefore believes that the negative conclusions of Freundlich, Joachimson, and Ettisch are not sufficiently justified, and thinks that Freundlich's original adsorption theory of the flocculation may still be correct in some respects.

As a result of our own work on the silver iodide sol, to be discussed in more detail in the next section, we came to the conclusion that Freundlich's original theory cannot be maintained as a general theory of flocculation and is only more or less valid for a few special cases.

For the better apprehension of our point of view we must first discuss the flocculation theory of Hans Müller (99), published almost simultaneously with the investigation of Freundlich to which we referred. According to Müller the first assumption of Freundlich's theory is not correct, namely, the assumption that flocculation is due to a decrease of the free charge of the particles. Previously this assumption had been considered to be so obvious that it had been accepted without definite proof.

Müller applied the theory of the diffuse layer of Gouy, Debye, and Hückel, discussed in Part I, and corrected it for the case of the particles being small and of colloidal size, i.e., for a strong curvature of the double layer. With the aid of this theory he calculated from electrophoretic data of Freundlich and Zeh (40) the corresponding charge of the particles. Freundlich and Zeh had measured very accurately the electrophoretic velocity of the particles of an arsenic trisulfide sol and the influence of small quantities of different electrolytes upon it. They varied the charge on the ion, and in order to have ions of a similar nature they used electrolytes with large complex cations. For this case the curves representing ζ as a function of the concentration of the electrolyte have a normal shape, i.e., ζ is lowered gradually at a decreasing rate while c is increasing.

Müller calculated these ζ - c curves for 1-1, 2-1, 3-1, and 4-1 valent electrolytes, assuming that the corresponding charge (i.e., the charge of the diffuse outer layer) was a *constant* throughout the whole concentration region. Then, giving to the particles an average charge of 86 electrons,

he found curves practically coinciding with the experimental curves of Freundlich and Zeh. Thus it is seen that the assumption of a decreasing charge is not necessary in order to explain a lowering of ζ , and consequently a decreasing secondary stability of a sol, when the concentration of electrolytes in the sol is raised. The theory of the diffuse double layer is able to explain the behavior of ζ as a function of c quantitatively, at least for a normal shape of the ζ - c curves. (Abnormal curves, e.g., with a maximum, will be discussed in a following section.)

It is easy to show that the theory of the diffuse layer also gives a very satisfactory explanation of Schulze-Hardy's rule. For this purpose we will avoid Müller's rather difficult mathematical treatment and restrict our reasoning, like Gouy's, to a flat double layer. We thus neglect the influence of the curvature of the double layer, which leads to much more simple formulas. In this case the differential equation, expressing the potential as a function of the concentration, has an exact solution. The approximation introduced by Debye and Hückel for the similar problem of the diffuse ionic sphere around an ion cannot be used for our case, since it holds only for $n\zeta < 25$ millivolts (n = charge of the ion considered, in our case the charge of the particle).

Let $\varphi(z)$ be the potential at a point (in the solution) that is at a distance z from the attaching layer. Using Poisson's equation, we have:

$$\frac{d^2\varphi}{dz^2} = -\frac{4\pi}{D} \rho$$

The density of the charge, ρ , is determined by the surplus of ions of one sign; if c denotes the concentration of the ions in equivalents per cm.³, F is the Faraday equivalent:

$$\rho = F(c_+ - c_-)$$

from which, with the aid of Boltzmann's theorem, is easily derived:

$$\left. \begin{aligned} \frac{d^2\varphi}{dz^2} &= -\frac{4\pi}{D} Fc \left\{ e^{\frac{-n_+ F\varphi}{RT}} - e^{\frac{+n_- F\varphi}{RT}} \right\} \\ \text{for } z = 0: \\ \varphi &= \zeta \text{ and } -\eta_2 = \int_0^\infty \rho dz = \frac{D}{4\pi} \left(\frac{d\varphi}{dz} \right)_0 \\ \text{for } z = \infty: \\ \varphi &= 0 \text{ and } \frac{d\varphi}{dz} = 0 \end{aligned} \right\} \quad (7)$$

The solution of equation 7 follows by integration, whence:

$$\eta_2 = \sqrt{\frac{DRTc}{2\pi}} \cdot \sqrt{\frac{1}{n_+} \left(e^{\frac{-n_+ F \zeta}{RT}} - 1 \right) + \frac{1}{n_-} \left(e^{\frac{+n_- F \zeta}{RT}} - 1 \right)} \quad (8)$$

With the aid of this equation we can calculate the amount of an n_+n_- -valent electrolyte that is necessary in order to lower the potential of a negative surface to $\zeta = -50$ millivolts. In this calculation we assume, in accordance with Müller, that the charge of the diffuse layer, η_2 , is a constant. The choice of -50 millivolts is somewhat arbitrary, but it is selected because under this condition $F\zeta/RT = -2$, and because the value is only slightly larger than the "critical potential" of most sols. Thus we calculate a concentration which will be a measure of the "flocculation value" of the electrolyte. As we do not know the exact value of η_2 we can only calculate the ratio between the various flocculation values. Therefore we choose arbitrarily the "critical" concentration for 1-1 valent electrolytes to be 50 millimoles per liter; the values for other types of electrolytes then follow easily from

$$c \left(\frac{1}{n_+} e^{+2n_+} + \frac{1}{n_-} e^{-2} \cdot \frac{n_+ + n_-}{n_+ n_-} \right) = \text{constant}$$

These values are summarized in the following table:

n_-	$n_+ = 1$	$n_+ = 2$	$n_+ = 3$	$n_+ = 4$
1	50	10.7	2.06	0.38
2	47	10.5	2.06	0.38
3	46	10.4	2.06	0.38
4	46	10.4	2.06	0.38

We see that the characteristic differences between various types of electrolytes, given by Schulze-Hardy's rule, actually result from the calculation. Electrolytes with unequally charged anions have almost the same flocculating action. The ratio between the "flocculation values" thus calculated for electrolytes with a mono-, di-, tri-, and tetra-valent cation is about 125:25:5:1. These concentrations, though expressed in equivalents, actually diverge greatly according to the valence of the ion with a charge opposite to that of the surface. The calculated ratios also correspond approximately to the ratios found experimentally. A strictly quantitative agreement cannot be expected, since we made some neglects and approximations; moreover, the theory still needs a few corrections, which will be discussed in the following sections.

Interchanging n_+ and n_- we can of course use the table for the case of a positively charged surface.

The physical interpretation of these regularities, derived formally from Gouy's theory, can be given easily. As a consequence of the negative charge of the surface, the positive ions in the solution are attracted and accumulated in the neighborhood of the surface and the negative ions are repelled. As we have discussed in Part I, section II, these electrical forces are counteracted by the thermal agitation of the ions, which leads to the picture of the diffuse outer charge. The formation of this positive space charge quite near the surface will be easiest when a large number of ions is available, i.e., when the solution is concentrated. Thus for large concentrations of the electrolytes in the solution, the "thickness" of the diffuse layer is less than for smaller concentrations. We can consider the double layer, as usual, as a condenser, and state that for a decreasing thickness its capacity increases, and for equal charges, its potential is lowered. The influence of the charge of the cations can be explained in a similar way. The higher this charge the more difficult it is to distribute the positive ions over some distance into the solution as a result of the thermal agitation; the smaller therefore is the thickness of the double layer and its ζ -potential.

The anions have the opposite tendency. By entering the outer layer they tend to enlarge the thickness of the diffuse outer charge and to raise the ζ -potential. However, it is only a small quantity that succeeds in reaching these layers. Nearly all of them are repelled by the negative surface, and more strongly so the higher their charge. The above equations indicate that the (integrated) amount of anions in the diffuse outer layer is represented by the second term under the square root in equation 8; this term is small for high values of ζ and n_- . For the case of a 2-2 valent electrolyte, $\zeta = -50$ millivolts; the ratio cation:anion amounts to $(e^4 - 1) : (1 - e^4) = 55:1$. The influence of the anions upon the potential is therefore almost negligible.

Obviously unaware of Müller's paper, Audubert (4) has recently tried to calculate ζ - c curves for different types of electrolytes with the aid of the theory of the diffuse layer. His results have a restricted value, since he erroneously used Debye-Hückel's approximation, valid only for $n\zeta < 25$ millivolts. Yet he also concludes from a comparison of calculated and observed ζ - c curves that, upon the addition of small amounts of electrolytes, the electrophoretic charge is a constant.

In summarizing, we state that the theory of the diffuse layer gives a satisfactory explanation of the secondary stability of lyophobic colloids in several respects. It is not necessary to assume that the particles are "neutralized" by an "adsorption"; on the contrary we can consider this charge, as a first approximation, to be a constant. The lowering of ζ as a result of addition of electrolytes is merely due to a "compression" of

the diffuse outer layer and a subsequent increase of the capacity of this part of the double layer.

Bull and Gortner (16) gave a method to determine the mobile part of the charge of the double layer. They combined measurements of the streaming potential and of the surface conductance, e.g., for cellulose in contact with solutions of different electrolytes. Thus they were able to calculate the variations of ζ and of the charge with varying concentrations. In the concentration region of 10^{-4} to 10^{-3} they found that the ζ -potential, though decreasing normally, is connected with a constant or even a slightly increasing charge.

The first assumption of Freundlich's original flocculation theory is thus definitely invalidated. What, then, was the significance and the function of the ions carried down by the flocculating particles? How can we explain that the amounts of these ions frequently were equivalent, but in other cases not equivalent?

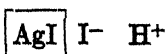
It is clear that these phenomena are not accounted for by Müller's theory. In trying to answer these questions, we will see that this theory needs a few corrections, and in some respects is too simple.

IV. INVESTIGATIONS WITH THE SILVER IODIDE SOL

In our opinion the silver iodide sol had several advantages for a study of the interaction of sol particles and indifferent flocculating electrolytes. The sol is well-defined chemically; the constituents of its double layer are known exactly; and we have seen that we can describe quantitatively the conditions of its primary stability. The aging of these sols has been studied extensively; in dialyzed sols, prepared in the proper way, this aging can be reduced to a minimum. Moreover, the aging and a subsequent change of the total charge of the particles can be controlled easily by the measurement of the free iodide-ion concentration in the sol.

Another favorable condition is that the charge of the particles is so extremely small. A practical disadvantage, however, is that the analytical measurements become much more difficult. The latter drawback could be overcome partly by using strongly concentrated sols (up to 40 per cent). Thus we could avoid difficulties arising eventually from the complication discussed at the end of Part I, section III. We have seen that for several sols there is an unexplained discrepancy between the total charges of the particles found analytically and calculated from the ζ -potential. In the case of the silver iodide sol, this complication seems to be absent.

The dialyzed silver iodide sols, as used in our experiments, contain hydrogen ion as counter-ions of the double layer



Electrolytes with different cations were added to the sols in varying amounts, and after a definite time the concentration of these cations was measured in the ultrafiltrate or (when complete flocculation had occurred) in the supernatant liquid. Incidentally it was shown that the cations "adsorbed" substituted an equivalent amount of hydrogen ion from the double layer.

We learned from these measurements (Verwey and Kruyt (126)) that sometimes the amount of cation "adsorbed" already reached a maximum for comparatively small concentrations of the ions, and did not increase any more with larger amounts of electrolytes added. Occasionally this maximum was reached for concentrations far below the flocculation region. This maximum proved to be about equivalent to the total amount of hydrogen ion in the double layer; the latter was determined by the electrochemical analysis of the sols after Pauli's methods. The upper limit of the "adsorption" of the cations is therefore determined by the total amount of exchangeable hydrogen ions available.

From this we can conclude that the "adsorption" of cation in all events is not *sufficient* to flocculate the negative sol, for sometimes complete "adsorption" occurs at much lower concentrations than correspond to the flocculation value. In other cases, flocculation occurred long before sufficient electrolyte was added in order to reach the maximum "adsorption." This was found for various kinds of cations if previously a large excess of hydrogen ion was added to the sols.

From our considerations in Part I, section V, it will be perfectly clear that the "adsorption" of cations by the negative particles is a pure exchange of counter-ions. Both exchanging ions play an equivalent part in the phenomenon. The exchange has no relation to the flocculation. Especially a variation of their electrophoretic charge during the exchange does not necessarily occur, in accordance with the opinions of Müller, Audubert, and Bull and Gortner.

In order to be precise in these conclusions we have stated that the phenomenon does not obey the "adsorption isotherm," equation 6 in Part I, section VI, but on the contrary an equation $x = f\left(\frac{c}{m}\right)$, which means that it is independent of the dilution. We have seen in Part I, section V, that this is exactly the criterion of an exchange of counter-ions. This proves that the third supposition in Freundlich's original theory is also contrary to the actual state of affairs. Our experiments mentioned above had already proved that the fourth supposition also was wrong for this type of "adsorption."

In Part I, section V, we have reproduced the various exchange tendencies of different cations by a sequence, in which generally the exchange tend-

ency proves to be larger for ions of higher valence. Within a group of ions of the same charge the larger ions exchange more strongly.

Of an ion added to the sol the amount taken up by the particles is thus determined by its position in this sequence, and, since we are dealing with an exchange, by the ratio of the amounts of exchanging and substituted ion. For dialyzed sols, if not too much diluted, the amount of free ions in the sol medium is negligible with regard to the ions present in the double layer. Thus the concentration of the ions, present in the sol as counter-ions (for silver iodide the hydrogen ions), is proportional to the sol concentration. The flocculation, however, occurs at a definite concentration of the free ions in the sol medium. Thus, for a given sol and a given electrolyte, it depends on the sol concentration how many of the ions added are taken up by the particles at the flocculation point.

This may be elucidated by figure 11, in which we plotted the amounts of lead ion "adsorbed" against the amounts added to the solution. The "adsorption" was determined (with ThB^{++} as radioactive indicator) for a dialyzed silver iodide sol and for the same sol diluted eleven times. The dotted line gives the curve for the diluted sol again on a scale eleven times larger. All concentrations are in milliequivalents per liter. Actually both curves have exactly the same shape, and nearly coincide. The small difference is due to two effects: in the first place some potential-determining electrolyte (HI) has been given back to the solution on account of the dilution, decreasing the total particle charge to a small amount; moreover the dilution is not exactly elevenfold but somewhat larger, as a consequence of the volume occupied by the silver iodide particles. The flocculation point of the concentrated sol is indicated in figure 11 by $\}$; we see that at this point the exchange is just about quantitative, and the maximum of the exchange is reached. The corresponding point of the curve for the diluted sol, however, represents a concentration of free lead ions which is eleven times smaller, i.e., a lead-ion concentration far below the flocculation region. The latter is given by a line ab , parallel to the straight line $x = y$; all lines of this type connect points of equal concentration of free lead ion.

We have already seen that for other sols the charge, and therefore the concentration of the counter-ions or the exchange capacity (T), is 100 to 1000 or more times as large as it is for silver iodide. In the experiments of Freundlich, Weiser, and Rabinowitch, discussed earlier (Part II, section III) the exchange capacity was therefore mostly larger than in ours, even when they used rather dilute sols. Frequently the case was realized that, at the flocculation point, the maximum of the exchange curve was reached scarcely or not at all. This is the explanation why the amounts "adsorbed" were sometimes equivalent, in other cases not.

Equivalent "adsorption" occurred when the sol concentration and other conditions were such that for all electrolytes the exchange was about complete.

In recent investigations by Weiser and Gray (135) and by Bolam and Bowden (13), carried out respectively with As_2S_3 and Odén sulfur sol, the curves for different electrolytes happen to have such a form that in both cases the investigators concluded that flocculation occurs when the substitution is complete. The theory of Weiser and Gray, developed on the basis of these experiments, is essentially identical with Freundlich's old theory which has already been rejected in the preceding section of this

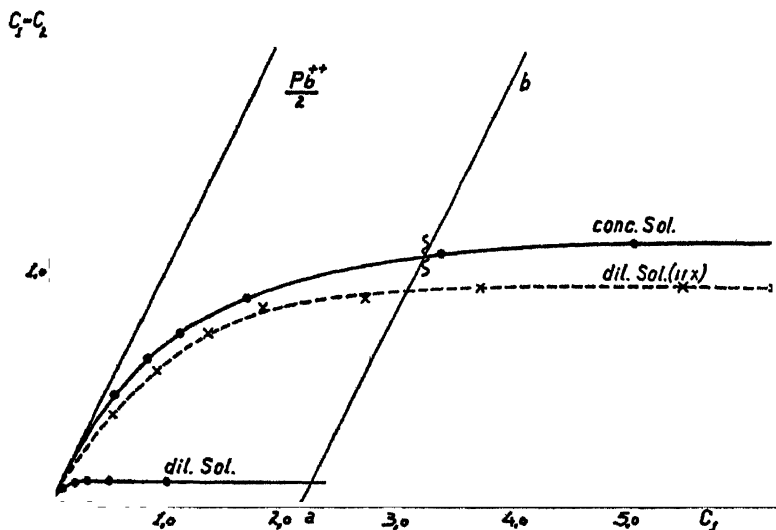


FIG. 11. Exchange isotherms $\text{Pb}^{++}/\text{H}^{+}$ with silver iodide sol. The curve for the concentrated sol is about the elevenfold multiplication of the curve for the sol diluted eleven times; this is characteristic for an exchange and not for an adsorption.

paper. From the experiments discussed above we have seen that a coincidence of the flocculation region and the point where the exchange is practically complete is not the general case, and therefore only accidental. Thus we may state that the considerations of Weiser and Gray and of Bolam and Bowden are not justified.

Rabinowitch and Kargin (108) have titrated conductometrically an arsenic trisulfide sol with barium chloride solution. A discontinuous change in the curve indicates the point where the hydrogen ion of the double layer has been substituted almost completely by the barium ion added. Rabinowitch and Wassiliev (109) recently stated that the sols to which this amount of barium chloride was added did not coagulate,

even if they were allowed to stand a long time. They conclude that two "phases" of the coagulation exist. Though this conclusion approaches that of ours we cannot quite agree with it. We have seen that the first "phase" of the coagulation, the exchange, is not at all necessary for the flocculation. The exchange may accompany the flocculation but is not essential for it.

V. EXCHANGE OF COUNTER-IONS AND COLLOIDAL BEHAVIOR

The exchange is not important for a general coagulation theory. In a special flocculation theory, however, it can not be neglected.

According to Müller's theory one would expect that all electrolytes of the same type (i.e., with the same values of n_+ and n_-) lower the potential and coagulate in exactly the same way. This is not true, for characteristic differences exist between electrolytes with, for instance, various ions charged oppositely to the sol. Provided that the particles are sufficiently lyophobic (Voet and Balkema (131)), we generally find that the flocculation action of equally charged ions increases with the ionic radius. Thus, for a positive sol $I^- > Br^- > Cl^- > F^-$; for a negative sol $Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$. The H^+ or H_3O^+ ion occupies a special position, and flocculates generally more strongly than Cs^+ .

Various explanations have been proposed for these phenomena. In our opinion it is easy to understand this behavior in the following way. The sequence found for the potential-lowering action of equally charged ions is exactly the same as the sequence found for the exchange. Those ions which strongly substitute other ions also have a stronger flocculating action. These phenomena are directly connected with each other. This is clear for an extreme case,—for the exceptions of Schulze's rule. Flocculating an arsenic trisulfide sol with new fuchsin, for instance, we need only an extremely small quantity of these ions. At the same time we can observe that the ion is taken up quantitatively by the double layer. If, however, when the flocculation has been effected, more of the new fuchsin chloride is added, the solution becomes colored immediately (Freundlich and Neumann (35)). Exactly the same has been found by Zsigmondy and Heinz (142) for the coagulation of a negative SnO_2 sol. Some electrolytes, as sodium or potassium salts, give normal values for the flocculation concentration. All polyvalent cations, and also silver ion, are exceptions to Schulze's rule. The amounts needed for coagulation are small, and depend solely on the amount of peptizing electrolyte (KOH) present in the double layer, i.e., they are equivalent to the amount of the peptizing ion. For this case, indeed, a chemical "interpretation" of the coagulation (formation of insoluble stannates, and therefore precipitation) seems to

give a good description of the facts. But we have already stressed the fact that this is an exceptional case (cf. Part II, section II).

In these cases we deal with ions that have a strong attraction toward the surface, and, for that reason, exchange other ions very strongly. In other words, these ions have a very large "adsorption potential" in the sense of Stern (cf. Part I, section III). According to Stern's theory these ions are drawn quantitatively into the "attaching" ionic layer ("Helmholtz layer"). Thus the ions added to the sol completely destroy the diffuse outer layer, and raise the charge η_1 at the cost of η_2 . This is actually a kind of "neutralization" of the particles, if one considers that only the electrophoretic charge η_2 is neutralized. For these extreme cases Freundlich's picture of flocculation remains valid, and becomes identical with that of Zsigmondy. But we notice that these pictures are right only when the flocculating ions are "adsorbed" almost quantitatively by the exchange of counter-ions, and the flocculation value is low and about proportional to the amount of peptizing ion (= exchange capacity).

These cases are not of the normal type of flocculation. The transition to the normal case is however a continuous one. The ions of the heavy metals, H_3O^+ , and OH^- , frequently occupy an intermediate position. The flocculation values of these ions are mostly considerably smaller than for the equally charged ions with the electronic structure of the inert gases (8- or helium-scale); they are not low enough to "precipitate" the sol particles by an almost complete exchange. Van Arkel and de Boer (5) have already pointed out that these comparatively low flocculation values must be explained by the large polarizabilities of the heavy metal ions and by the dipoles of H_3O^+ and OH^- .

To a smaller extent these specific influences are still present for the ions with a 8-electronic scale. Their polarizabilities, though smaller, vary considerably. We must correct Müller's theory (in which the electrophoretic charge was considered to be independent of the electrolyte and its concentration) in such a way that we take into account the variations of the charge of the diffuse layer. This charge is determined by the distribution of the counter-ions over the diffuse and the "Helmholtz" layer. If we add electrolyte to the sol an exchange of the counter-ions occurs; the composition of the outer layers is changed. Generally there will be a shift of the equilibrium of counter-ion distribution over both layers (independent of changes of this equilibrium by the change of the total electrolyte concentration which are equal for all electrolytes of the same type). Generally speaking the electrophoretic charge (which determines the ζ -potential) is not a constant, but may either increase or decrease.

If the ion added to the sol has a larger adsorption potential (ϕ) than the counter-ion of the double layer, the charge η_2 will always decrease,

intensifying the normal decrease of ζ . In the opposite case the exchange is small, but the ions entering the double layer cause an opposite shift of the charges, increasing the charge η_2 . This increase of the electrophoretic charge will perhaps not lead to an initial increase of ζ , for the latter is lowered at the same time by the increased concentration. At any rate the potential will be lowered less than for ions with larger values of ϕ .

The adsorption potential, ϕ , and therefore the exchange is governed, for ions of the simple type, by their polarizability. Since the latter increases considerably in the sequences $\text{Li} \rightarrow \text{Cs}$ and $\text{F} \rightarrow \text{I}$, the flocculating action of these ions will increase in the same direction.

In this way we can give plausible explanations for the characteristic variations among various flocculating ions of the same valence.⁹

The exchange of counter-ions is still important for another group of phenomena. It reveals the relation between the flocculation value and the sol concentration. It is clear that the probability of collision and therefore the rate of flocculation will decrease after dilution of the sol. This factor has been discussed by Kruyt and van der Spek (77) and Fodor and Riwlín (42), but its influence upon the change of the flocculation value with varying sol concentration must be small (cf. Weiser and Nicholas (137)). By dilution of the sol the total exchange capacity per liter is diminished. The amount of electrolyte required for flocculation therefore decreases when the ion added flocculates more strongly than the counter-ion of the sol. In the opposite case the flocculation value of the electrolyte will be increased upon the dilution of the sol.

When a dialyzed silver iodide sol is treated with ceric nitrate, the Ce^{3+} is taken up by the particles almost quantitatively until the maximum exchange is reached. A very concentrated dialyzed silver iodide sol, with an exchange capacity of 1.34 milliequivalents per kilogram of sol, required for its flocculation about 1.6 milliequivalents of Ce^{+++} ; the flocculation value for a more diluted sol with an exchange capacity of 0.18 milliequivalent was only 0.4 milliequivalent (Verwey and Kruyt (126)). The free concentration of Ce^{+++} was therefore at the moment of flocculation about 0.2 milliequivalent per liter in both cases. For "normal" sols, i.e., for sols with a particle charge some powers of ten times as large as that of silver iodide sol, the exchange capacity is so large that similar effects will already occur in dilute sols. The effect will also increase with the charge of the ion, as generally the exchange tendency is large for ions of high valencies. The experimental facts (see also the work of

⁹ *Note added in proof:* In a recent paper H. Jenny and R. F. Reitemeier (J. Phys. Chem. 39, 593 (1935)) have discussed the relation between ionic exchange and stability of lyophobic colloids in a similar way. Their treatment differs only slightly from ours. In some details we prefer the formulations chosen above.

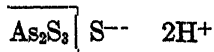
Burton (19), Freundlich (39), Ghosh and Dhar (29), and Usher (121)) seem to substantiate the above views.

VI. PURE ADSORPTION OF ELECTROLYTES AND COLLOIDAL BEHAVIOR

We have considered the significance of potential-determining electrolytes for colloid chemistry and examined the influence of counter-ionic exchange when indifferent electrolytes are added to a sol. In our previous review we have, however, neglected the pure adsorption of electrolytes. For several sols, especially for the silver iodide sol, this was perfectly allowable. That the phenomena were found to be rather simple for this sol was probably partly due to the circumstance that silver iodide does not adsorb foreign electrolytes (Beekley and Taylor (7)). Actually we found no indication of pure adsorption and observed only an equivalent ionic exchange. The analytical results of Freundlich, Joachimson, and Ettisch, discussed in a previous section (Part II, section III), prove, however, that in the case of the arsenic trisulfide sol and gold sol, the phenomena are complicated by a pure adsorption of the electrolytes.

The available data seem to be insufficient to discuss this problem in detail, especially in connection with the stability and other properties of the sol. However, we can give some general points of view which have to be considered fully in order to have a better understanding of these rather complicated phenomena.

Let us consider, for example, the double layer of arsenic trisulfide sol:



An electrolyte is added, say potassium chloride, which is indifferent since it does not change the total potential of the double layer. In the first place an exchange of some hydrogen ion by potassium ion occurs; we have seen that this does not change the double layer fundamentally. Moreover, the potassium chloride is adsorbed, and we will assume that in this process the chloride ion is the leading ion. Thus there will be an orientation of charges in the outer layer of the double layer, and this will cause a transportation of S^{--} ions to the solution (cf. Part I, section VI), as a consequence of the shift of the zero point of surface charge. The concentration of S^{--} in the sol medium is increased, and the total potential of the double layer becomes more negative. The potential slope in the double layer and therefore ζ is changed in a rather complicated way.

From the work of Kruyt, Janssen, and others, discussed in Part I, section VI, we learn that a strong adsorption of anions by a negative sol leads to a maximum in the ζ - c curve. Such a maximum is always an

indication that adsorption occurs. The same is true for electrolytes which are able to reverse the charge of a sol ("irregular series"); for instance, it is a well-known fact that a negative gold sol can be charged positively by Th^{++++} . Here apparently the cations go into the "attaching" layer so strongly that their total charge surpasses that of the gold particles. The compensating charge of the diffuse layer then becomes negative. We have therefore the case of figure 7, with the opposite signs only. A more quantitative treatment of these phenomena meets with serious difficulties. Moreover, the discontinuity of the changes (Part I, section III) may be here of considerable importance (see the discussion of Frumkin (44, pp. 255-6)).

VII. SUMMARY

In Part I we have studied the properties of the electrical double layer and the "adsorption" of electrolytes. In Part II we have tried to apply our theoretical considerations to the problems of the stability of lyophobic colloids. The general relationships for this "stability" have been discussed, both from the thermodynamic and the kinetic point of view. The conditions for primary stability (peptization) and secondary stability (coagulation) have been studied especially. These phenomena are not "stabilities" in the absolute sense and must be clearly distinguished from "coarsening" of the sol particles. A concept of general validity has been given of the fundamental significance of the potential-determining electrolytes for the primary stability. With the aid of this principle, the theory of peptization has been discussed. An extensive survey of the theory of coagulation has been given, including the original theory of Freundlich and more modern concepts on the basis of the theory of the double layer. We have tried to indicate the limitations of these theories and to arrive at a synthesis. The corrections that are still necessary (in order to take into account the exchange of counter-ions and the pure adsorption of electrolytes) have also been discussed briefly.

In conclusion I wish to express my thanks to Prof. Dr. H. R. Kruyt (Utrecht), Prof. Dr. I. M. Kolthoff (Minneapolis), and Dr. J. H. de Boer (Eindhoven) for their valuable help and interest in the preparation of this paper.

REFERENCES

- (1) ABRAMSON, H. A., AND MÜLLER, H.: *Proc. Am. Phys. Soc.* 7, 11 (1932).
- (2) ANDAUER, M., AND LANGE, E.: *Z. physik. Chem.* 156A, 241 (1931).
- (3) ANDAUER, M., AND LANGE, E.: *Z. physik. Chem.* 166A, 219 (1933).
- (4) AUDUBERT, R.: *J. chim. phys.* 30, 89 (1933).

- (5) VAN ARKEL, A. E. AND DE BOER, J. H.: *Chemische Bindung*. S. Hirzel, Leipzig (1931). Also in French translation, considerably revised, to appear before long (Serie: Le livre scientifique, Paris).
- (6) BASINSKI, A.: *Kolloid Beihefte* **36**, 258-349 (1932).
- (7) BEEKLEY, J. S., AND TAYLOR, H. S.: *J. Phys. Chem.* **29**, 942 (1925).
- (8) DE BOER, J. H.: *Z. physik. Chem.* **14B**, 149, 457; **15B**, 281, 300; **16B**, 397; **17B**, 161 (1932).
- (9) DE BOER, J. H., AND DIPPPEL, C. J.: *Z. physik. Chem.* **21B**, 198, 278 (1933); **25B**, 399 (1934).
- (10) DE BOER, J. H., AND CUSTERS, J. F. H.: *Z. physik. Chem.* **21B**, 208 (1933); **25B**, 225, 238 (1934).
- (11) DE BOER, J. H., AND LEHR, J. J.: *Z. physik. Chem.* **22B**, 423 (1933); **24B**, 98 (1934).
- (12) DE BOER, J. H., AND VEENEMANS, C. F.: *Physica* **1**, 573, 953, 960 (1934).
- (13) BOLAM, TH. R., AND BOWDEN, G.: *J. Chem. Soc.* **1932**, 2684.
- (14) BRAGG, W. L.: *Z. Krist.* **74**, 237 (1930).
- (15) DE BROUCKÈRE, L.: *J. chim. phys.* **25**, 605 (1928); **26**, 250 (1929); **27**, 543 (1930).
- (16) BULL, H. B., AND GORTNER, R. A.: *J. Phys. Chem.* **35**, 309 (1931).
- (17) BUNGENBERG DE JONG, H. G.: *Rec. trav. chim.* **42**, 437 (1923); **43**, 35 (1924).
- (18) BURTON, E. F., AND ANNETTS, MAY: *J. Phys. Chem.* **35**, 48 (1931).
- (19) BURTON, E. F., AND BISHOP, E.: *J. Phys. Chem.* **24**, 701 (1920).
BURTON, E. F., AND McINNES, E. D.: *J. Phys. Chem.* **25**, 517 (1921).
- (20) BURTON, E. F.: *Phil. Mag.* [6] **11**, 440 (1906).
- (21) BURGERS, W. G., AND DIPPPEL, C. J.: *Physica* **1**, 549 (1934).
- (22) CHAPMAN, D. L.: *Phil. Mag.* [6] **25**, 475 (1913).
- (23) COEHN, A.: *Wied. Ann.* **64**, 217 (1898).
- (24) COEHN, A., AND RAYDT, U.: *Ann. Physik* [4] **30**, 777 (1909).
- (25) CYSOUW, H. A.: *Dissertation*, Utrecht, 1934.
- (26) DANIEL, JANET: *J. Gen. Physiol.* **16**, 547 (1933).
- (27) DEBYE, P., AND HÜCKEL, E.: *Physik. Z.* **24**, 185, 305 (1923).
DEBYE, P.: *Trans. Faraday Soc.* **23**, 334 (1927).
- (28) DEBYE, P., AND HÜCKEL, E.: *Physik. Z.* **25**, 49 (1924).
- (29) DHAR, D. R., AND GHOSH, S.: *J. Phys. Chem.* **31**, 187, 649 (1927).
- (30) ELISSAFOFF, V.: *Z. physik. Chem.* **79**, 385 (1912).
- (31) FAJANS, K., AND VON BECKERATH: *Z. physik. Chem.* **97**, 478 (1921).
- (32) FAJANS, K., AND ERDEY-GRÚZ, T.: *Z. physik. Chem.* **158A**, 97-151 (1932).
- (33) FREUNDLICH, H.: *Kapillarchemie*, 4th edition, with J. Bikerman. Akademische Verlagsgesellschaft, Leipzig (1930).
- (34) FREUNDLICH, H.: *Kolloid-Z.* **1**, 321 (1907); *Z. physik. Chem.* **73**, 385 (1910).
- (35) FREUNDLICH, H., AND NEUMANN, W.: *Z. physik. Chem.* **67**, 538 (1909).
- (36) FREUNDLICH, H., AND SCHUCHT, H.: *Z. physik. Chem.* **85**, 641 (1913).
- (37) FREUNDLICH, H., AND HAASE, E.: *Z. physik. Chem.* **89**, 417 (1915).
- (38) FREUNDLICH, H., AND GANN, J. A.: *Kolloidchem. Beihefte* **8**, 127 (1916).
- (39) FREUNDLICH, H., AND LOENING, E.: *Kolloidchem. Beihefte* **16**, 1 (1922).
- (40) FREUNDLICH, H., AND ZEH, P.: *Z. physik. Chem.* **114**, 65 (1924).
- (41) FREUNDLICH, H., JOACHIMSON, K., AND ETTISCH, E.: *Z. physik. Chem.* **141A**, 249 (1929).
- (42) FODOR, E., AND RIWLIN, R.: *Kolloid-Z.* **44**, 69 (1928).
- (43) FRUMKIN, A.: *Z. physik. Chem.* **109**, 34 (1924).
- (44) FRUMKIN, A.: *Sow. Phys.* **4**, 239 (1933).
- (45) FRUMKIN, A.: *Ergebnisse der exakten Naturwissenschaften* **7**, 235 (1928).

- (46) FRUMKIN, A., AND PROSKURNIN, M.: *Z. physik. Chem.* **155A**, 29 (1932).
- (47) GANSSEN, R.: *Centr. Mineral. Geol.* **1913**, 699, 728.
- (48) GIBBS, J. W.: *Thermodynamics*. Longmans, Green and Co., London and New York (1906).
- (49) GOUY, G.: *Ann. chim. phys.* [7] **29**, 145-241 (1903).
- (50) GOUY, G.: *J. phys.* [4] **9**, 457 (1910); *Ann. Physik.* [9] **7**, 129 (1917).
- (51) GYEMANT, A.: *Z. Physik* **17**, 190 (1923).
- (52) GYEMANT, A.: *Kolloidphysik*. F. Vieweg and Son, Braunschweig (1925).
- (52a) HABER, F., AND BEUTNER, R.: *Ann. Physik* [4] **26**, 947 (1908).
- (53) HAHN, O., AND IMRE, L.: *Z. physik. Chem.* **144A**, 161 (1929).
- (54) HARDY, W. D.: *Z. physik. Chem.* **33**, 385 (1900).
- (55) HELMWIG, K.: *Z. anorg. allgem. Chem.* **25**, 180 (1900).
- (56) HELMHOLTZ, W.: *Pogg. Ann.* **89**, 211 (1853); *Wied. Ann.*, N. F., **7**, 339 (1879).
- (57) HENRY, D. C.: *Proc. Roy. Soc. London* **133A**, 106 (1931).
- (58) HERZFELD, K. F.: *Physik. Z.* **21**, 28, 61 (1920).
- (59) HOROVITZ, K., AND PANETH, F.: *Z. physik. Chem.* **89**, 513 (1915).
- (60) HÜCKEL, E.: *Physik. Z.* **25**, 204 (1924).
- (61) IMRE, L.: *Z. physik. Chem.* **146A**, 41 (1930); **153A**, 127, 262 (1931); **164A**, 327, 343, 364 (1933); *Z. Elektrochem.* **38**, 534 (1932).
- (62) JAEGER, F. M.: *Trans. Faraday Soc.* **25**, 320 (1929).
JAEGER, F. M., WESTENBRINK, H. G. K., AND VAN MELLE, F. A.: *Proc. Acad. Sci. Amsterdam* **30**, 249 (1927); **32**, 167 (1929).
- (63) JENNY, H.: *Kolloidchem. Beihefte* **23**, 428 (1928); *J. Phys. Chem.* **36**, 2217 (1932).
- (64) JANSSEN, L. W.: *Sow. Phys.* **4**, 322 (1933); *Dissertation*, Utrecht, 1933.
- (65) JULIEN, P. F. J. A.: *Dissertation*, Utrecht, 1933.
- (66) KELLEY, W. P., DORE, W. H., AND BROWN, S. M.: *Soil Science* **31**, 25 (1931).
- (67) KING, J. F., AND PINE, P. R.: *J. Phys. Chem.* **37**, 851 (1933).
- (68) KOLTHOFF, I. M.: *Rec. trav. chim.* **46**, 549 (1927).
- (69) KOLTHOFF, I. M.: *J. Phys. Chem.* **36**, 860 (1932); *Chem. Weekblad* **29**, 332, 362 (1932).
- (70) KOLTHOFF, I. M., AND ROSENBLUM, CH.: *J. Am. Chem. Soc.* **55**, 2656, 2665 (1933).
- (71) KOLTHOFF, I. M., AND SANDELL, E. B.: *J. Am. Chem. Soc.* **55**, 2170 (1933).
- (72) KOLTHOFF, I. M., AND ROSENBLUM, CH.: *Phys. Rev.* **45**, 341 (1934).
- (73) KOLTHOFF, I. M., VON FISCHER, W., AND ROSENBLUM, CH.: *J. Am. Chem. Soc.* **56**, 832 (1934).
- (74) KRUYT, H. R.: *Colloids*, 2nd edition. Wiley and Sons, New York (1930).
- (74a) KRUYT, H. R.: *Sow. Phys.* **4**, 295 (1933).
- (74b) KRUYT, H. R.: *Bull. soc. chim. Belg.* **43**, 559-96 (1934).
- (75) KRUYT, H. R.: in *Alexander's Colloid Chemistry*, Vol. I, pp. 305-22. D. Van Nostrand Co., New York (1926).
- (76) KRUYT, H. R., AND VAN ARKEL, A. E.: *Kolloid-Z.* **32**, 29 (1923).
- (77) KRUYT, H. R., AND VAN DER SPEK, J.: *Kolloid-Z.* **25**, 1 (1919).
- (78) KRUYT, H. R.: *Kolloid-Z.* **22**, 81 (1918).
KRUYT, H. R., AND VAN DER WILLIGEN, P. C.: *Kolloid-Z.* **45**, 307 (1928).
- (79) KRUYT, H. R., AND BRIGGS, D. R.: *Proc. Acad. Sci. Amsterdam* **32**, 384 (1929).
- (80) KRUYT, H. R., AND VAN DER WILLIGEN, P. C.: *Z. physik. Chem.* **139**, 53 (1928).
- (80a) KRUYT, H. R., AND CYSOUW, H. A.: *Z. physik. Chem.* **172A**, 49, 56 (1935).
- (81) VAN LAAR, J. J.: *Lehrbuch der theoretischen Elektrochemie*, (1907).
- (82) LANGE, E., AND BERGER, R.: *Z. Elektrochem.* **36**, 171 (1930).

- (83) LANGE, E., AND BERGER, R.: *Z. Elektrochem.* **36**, 980 (1930).
(84) LANGE, E., AND BERGER, R.: *Z. physik. Chem.* **147A**, 470 (1930).
(85) LANGE, E., AND CRANE, P. W.: *Z. physik. Chem.* **141A**, 225 (1929).
(86) LANGE, E., AND MISCENKO, P. W.: *Z. physik. Chem.* **149A**, 1-42 (1930).
(87) LANGE, E.: *Handbuch der Experimentalphysik*, Vol. XII, 2, p. 265. Akademische Verlagsgesellschaft, Leipzig (1934).
(88) LANGMUIR, I.: *J. Am. Chem. Soc.* **38**, 2221 (1916); **40**, 1361 (1918); *Phys. Rev.* **6**, 79 (1915); **8**, 149 (1916).
(89) LEWIS, W. C. M.: *Trans. Faraday Soc.* **28**, 597 (1932).
(90) LINDER, S. E., AND PICTON, H.: *J. Chem. Soc.* **67**, 148 (1892); **67**, 62 (1895); **71**, 568 (1897).
(91) LOTTERMOSER, A.: *Z. physik. Chem.* **60**, 451 (1907); *Kolloid-Z. (Erg.-Bd.)* **36**, 230 (1925).
(91a) LOTTERMOSER, A., AND RIEDEL, W.: *Kolloid-Z.* **51**, 30 (1930).
(92) MARCH, A.: *Kolloid-Z.* **45**, 97 (1928).
(93) MOONEY, M. M.: *J. Phys. Chem.* **35**, 331 (1931).
(94) MUKHERJEE, J. N., AND KUNDU, P. W.: *J. Indian Chem. Soc.* **3**, 335 (1926).
(95) MUKHERJEE, J. N., BASU, J. K., AND MUKHERJEE, A.: *J. Indian Chem. Soc.* **4**, 459 (1927).
(96) MICHAELIS, L., TIMENEZ-DIAZ, C., AND HIRABAYASHI, N.: *Kolloid-Z.* **29**, 184 (1921); **30**, 209 (1922).
(97) MICHAELIS, L.: *Die Wasserstoffionen Konzentration*. J. Springer (1914).
(98) MICHAELIS, L., AND RONA, P.: *Biochem. Z.* **97**, 57 (1919).
(99) MÜLLER, H.: *Kolloidchem. Beihefte* **26**, 257 (1928).
(100) PAULI, Wo., AND VALKÓ, E.: *Elektrochemie der Kolloide*. J. Springer, Wien (1929).
(100a) PAULI, Wo.: *Naturwissenschaften* **30**, 555 (1932).
(101) PAULING, L.: *Z. Krist.* **74**, 213 (1930); *Proc. Nat. Acad. Sci.* **16**, 453 (1930).
(102) PERRIN, J.: *J. chim. phys.* **2**, 601 (1904); **3**, 50 (1905).
(103) POWIS, F.: *Z. physik. Chem.* **89**, 91, 189 (1915).
(104) PRAUSNITZ, P. H.: *Kolloid-Z.* **51**, 359 (1930).
(105) RABINOWITCH, A. J.: *Z. physik. Chem.* **116**, 97 (1925).
(106) RABINOWITCH, A. J., AND KARGIN, V. A.: *Z. physik. Chem.* **133**, 203 (1928).
(107) RABINOWITCH, A. J., AND FODIMANN, E.: *Z. physik. Chem.* **159A**, 403 (1932).
(108) RABINOWITCH, A. J., AND KARGIN, V. A.: *Z. physik. Chem.* **143A**, 21 (1929).
(109) RABINOWITCH, A. J., AND WASSILIEV, D. TH.: *Kolloid-Z.* **60**, 268 (1932).
(110) RABINOWITCH, A. J.: *Sov. Phys.* **4**, 304 (1933).
(111) RICE, O. K.: *J. Phys. Chem.* **30**, 189, 1348, 1660 (1926).
(112) ROTHMUND, V., AND KORNFELD, G.: *Z. anorg. allgem. Chem.* **103**, 129 (1918); **108**, 215 (1919).
(113) SCHULZE, H.: *J. prakt. Chem.* [2] **25**, 431 (1882); **27**, 320 (1883).
(113a) SMEKAL, A.: *Z. angew. Chem.* **42**, 489 (1929).
(114) VON SMOLUCHOWSKI, M.: *Graetz' Handbuch der Elektrizität und des Magnetismus* **2**, 366 (1914).
(115) VON SMOLUCHOWSKI, M.: *Physik. Z.* **17**, 557, 583 (1916); *Z. physik. Chem.* **92**, 129 (1918).
(116) STERN, O.: *Z. Elektrochem.* **30**, 508 (1924).
(117) TAYLOR, H. S.: *Proc. Roy. Soc. London* **108**, 105 (1925).
(118) TAYLOR, W. H.: *Z. Krist.* **74**, 1 (1930).
(119) TARTAR, H. V., AND GAILLEY, Z. J.: *J. Am. Chem. Soc.* **44**, 2212 (1922).
(120) TARTAR, H. V., AND DRAVES, C. J.: *J. Phys. Chem.* **30**, 763 (1926).

- (121) USHER, F.: *Trans. Faraday Soc.* **21**, 406 (1925).
- (122) VAGELER, P.: *Der Kationen- und Wasseraushalt des Mineralbodens.*
S. Hirzel, Leipzig (1932).
- (123) VERWEY, E. J. W.: *Proc. Acad. Sci. Amsterdam* **36**, 225 (1933).
- (124) VERWEY, E. J. W., AND KRUYT, H. R.: *Z. physik. Chem.* **167A**, 137 (1933).
- (125) VERWEY, E. J. W., AND KRUYT, H. R.: *Z. physik. Chem.* **167A**, 149 (1933).
- (126) VERWEY, E. J. W., AND KRUYT, H. R.: *Z. physik. Chem.* **167A**, 312 (1934).
- (127) VERWEY, E. J. W.: *Rec. trav. chim.* **53**, 933 (1934).
- (128) VERWEY, E. J. W.: *Chem. Weekblad* **31**, 789 (1934).
- (129) VERWEY, E. J. W.: *Natuurwetenschappelijk Tijdschrift* **7**, 89 (1934).
- (130) VERWEY, E. J. W.: *Dissertation, Utrecht*, 1934.
- (131) VOET, A., AND BALKEMA, F.: *Rec. trav. chim.* **52**, 371 (1933).
- (132) VON WEIMARN, P. P.: *Repts. Imp. Ind. Research Inst. Osaka Japan* **12**, 5, pp. 1-148 (1931).
- (133) WEISER, H. B.: *J. Phys. Chem.* **35**, 1, 1368 (1931).
- (134) WEISER, H. B., AND GRAY, G. R.: *J. Phys. Chem.* **36**, 2178 (1932).
- (135) WEISER, H. B., AND GRAY, G. R.: *J. Phys. Chem.* **36**, 2796 (1932).
- (136) WEISER, H. B.: in *J. Alexander's Colloid Chemistry*, Vol. I, p. 600. D. Van Nostrand Co., New York (1926).
- (137) WEISER, H. B., AND NICHOLAS, O.: *J. Phys. Chem.* **25**, 742 (1921).
- (138) WHITNEY, W. R., AND OBER, J. E.: *J. Am. Chem. Soc.* **23**, 842 (1901).
- (139) WIEGNER, G.: *Kolloid-Z.* **36A**, Zsigmondy Festschrift, pp. 341-69 (1925).
- (140) WIEGNER, G., AND JENNY, H.: *Kolloid-Z.* **42**, 268 (1927).
- (141) VAN DER WILLIGEN, P. C.: *Dissertation, Utrecht*, 1927.
- (142) ZSIGMONDY, G.: *Kolloidchemie.* Otto Spamer, Leipzig (1920).

METRICAL REPRESENTATION OF SOME ORGANIC STRUCTURES BY QUANTITATIVE X-RAY ANALYSIS¹

J. MONTEATH ROBERTSON

Royal Institution, London, W. 1, England

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I. INTRODUCTION

The central problem of x-ray structural analysis is to determine the position in space of the atoms in the unit cell of the crystal. For most organic crystals this unit contains only a few chemical molecules, so it will be seen that the problem in its final aspect becomes similar to one of the major problems of chemistry, viz., the determination of the space arrangement of the atoms in the molecule. The difference, however, is significant. The chemical problem in general requires a knowledge of the *relative* arrangement and position of the atoms and bonds, but the complete solution of the x-ray problem demands in addition a quantitative knowledge of the electron distribution and of the interatomic distances involved, not only for one molecule but for that small group of molecules which together make up the crystal unit.

The x-ray problem is in fact so complicated for most organic compounds that it is usually quite impossible to solve it by starting from the x-ray data alone. It would involve the simultaneous evaluation of a number of parameters which might vary from a few dozen to a few hundred, while the absence of any atom of predominant scattering power is often an added complication. But there is no need to attempt this almost impossible task. It is much better to join forces with the chemist and make use of the extensive body of knowledge which already exists in the structural formulas of organic chemistry. If the structural formula is accepted as a basis, it then remains to make this framework metrical and find its orientation in the crystal. The chemist is perhaps not much concerned with the orientation of the molecule in the crystal, but unfortunately this aspect cannot be disentangled from the process of working out the quantitative details of the formula itself, a matter which is of the greatest interest to the chemist and physicist alike.

¹ Based on a paper read to the Chemical Society (London) at Manchester, England, on November 9, 1934.

In the actual process of analysis, then, it is usually convenient to start with a rough model embodying the knowledge we already possess regarding the molecule. By a "model" in this sense we need imply nothing more concrete than a concise mathematical expression of the relative positions of the scattering centers and probable order of the interatomic distances involved. We then proceed to find, by a process of trial and error, how this model, or a combination of such models, if the crystal unit contains more than one molecule, must be oriented with respect to the crystal axes in order to explain the intensities of the principal x-ray spectra. Such preliminary work is often facilitated by a knowledge of the optical and magnetic properties of the crystal. When an approximate solution has been obtained in this way there is usually no doubt as to its validity, because although the number of parameters involved is large, the number of equations determining these parameters is always much greater.

The structure reached in this manner is of great interest because it represents a confirmation of the structural formula by a method which is utterly different from the methods of organic chemistry. We may find, as in the case of anthracene, that the structure can be explained by means of three interlocked hexagonal rings of atoms of radius 1.3 to 1.6 A.U. These rings may be flat or they may be slightly buckled, and we can find approximately their orientation in the crystal. But the most interesting part of the work begins when we try to push the results further than this. If we can deduce the structure exactly, then different types of linkage between the atoms, single and double bonds, will probably reveal themselves by involving slightly different interatomic distances, and we shall be able to gain precise information about such important matters as valency angles, and so on. In brief we shall be able to place the structural formulas of organic chemistry on an exact metrical basis.

Now in practice it is not usually possible to obtain such detailed information by an extension of the method of trial and error which we have used to obtain the broad outline of the structure. In the case of anthracene just mentioned, a buckling of the carbon rings appears to improve the calculated results for many of the reflections. But again, the conception of a larger central ring, combined with a small change in the orientation, would seem to improve the agreements for other reflections. It is in fact quite impossible to study systematically all the small changes which might be wrought on our working model.

Fortunately, however, when the work reaches this stage the problem can be approached in another way, by the method of Fourier analysis.²

² The method of the Fourier series as applied to crystal analysis was suggested by W. H. Bragg (Phil. Trans. **215A**, 253 (1915)), and further developed by Duane (Proc.

Each x-ray reflection given by the crystal can be thought of inversely as representing a certain average sinusoidal distribution of scattering matter, or electron density, running through the crystal, whose amplitude can be related to the measured intensity of the reflection. By combining the distributions obtained from all the reflections we can measure, it is possible to build up a more or less complete picture of the structure. Expressed mathematically, the intensity of each reflection enables us to calculate the coefficient of the corresponding term in a triple Fourier series which expresses the average electron density at every point in the crystal.

There are, unfortunately, many difficulties in the method, the most fundamental being our ignorance of, or rather the impossibility of measuring, the phase constant which belongs to each term in the series. Only the magnitude of the reflection can be measured. But this is just when the chemist comes to the rescue. The approximate solution which we have already determined by making the fullest use of our existing knowledge of the molecule is sufficiently accurate to determine the phase constants for most of the reflections which in practice it is possible to measure. It is then possible to apply the Fourier analysis, and its application leads to a considerable refinement of the results already obtained. For example, the different possibilities which we mentioned in the case of the anthracene structure are all found to lead to the same values for the phase constants (which can only be 0 or π for centrosymmetrical structures³). Therefore,

Nat. Acad. Washington 11, 489 (1925)), Havighurst (Proc. Nat. Acad. Washington 11, 502 (1925)), Compton ("X-Rays and Electrons," p. 151 (1926)), and W. L. Bragg (Proc. Roy. Soc. 123A, 537 (1929); *The Crystalline State*, Vol. I, p. 221 (1933)). Reference should be made to these works for full mathematical details of the method.

The series which represents the electron density, ρ , as projected along any direction in the crystal, for example, along the a -axis of a centrosymmetrical monoclinic crystal, is

$$\rho(y, z) = \frac{1}{bc \sin \beta} \sum_{-\infty}^{+\infty} \sum_{-\infty}^{+\infty} F(0kl) \cos 2\pi(ky/b + lz/c)$$

$F(0kl)$ is the "structure factor" of the reflection $(0kl)$, that is, the ratio of the wave amplitude scattered by the whole contents of the unit cell to that which would be scattered by a single electron under the same conditions. It is a quantity whose magnitude can be calculated from the measured intensity of the x-ray reflection; the experimental side of x-ray crystal analysis thus consists largely in making accurate determinations of F . But the sign of F , whether positive or negative, represents the "phase constant" of the reflection, and can only be determined by preliminary trial and error analysis.

³ If the structure as a whole has a center of symmetry, then this symmetry must apply to each component sinusoidal distribution of density which goes to build up the structure in the Fourier synthesis. Thus either the trough or the peak of each such distribution must coincide with the center of symmetry. Any intermediate position would destroy this symmetry.

the final result obtained by the application of this method is independent of the precise nature of the initial assumptions. We are justified in saying that the method of Fourier analysis renders possible a direct approach to the finer details of the structure.

This statement, however, must be immediately qualified by adding "but not too fine detail." We employ a series to represent the structure, and this series is, of course, never quite complete. It is artificially terminated at some point by the experimental conditions (limitation of wave length, etc.). If some terms of appreciable magnitude are excluded from our series, the resulting picture of the structure will be deficient, and may also include some false detail. This question has been carefully examined by Bragg and West (6). Most organic compounds, however, have a low melting point, and consequently the atoms in the crystal have a considerable thermal movement. This movement has the effect of smearing out the picture to some extent, with the result that the series are usually found to be naturally convergent within the region covered by the experiment.

Bearing in mind these shortcomings of the method we may now go on and consider some of the results which have been obtained by the application of this intensive method of analysis to certain well-known organic compounds. The choice of compounds may seem rather odd and perhaps uninteresting to the organic chemist, but in selecting the compound for detailed analysis we must be guided by many considerations. Reasonably good *single* crystals are, of course, usually essential, though they may be quite small. This at once excludes, or renders very difficult, the examination of many interesting compounds, particularly simple structures containing only a few atoms, which are nearly always liquids or gases at the ordinary temperature. Again, even when provided with good crystals, preliminary examination often shows the structure to be unexpectedly complicated, in that many molecules are built together into the crystal unit (which must be dealt with as a whole). The complication in this case is perhaps more apparent than real, but it does greatly increase the experimental and also the numerical work involved, so for the time being the consideration of such structures has been deferred.

In the examples which follow the crystals are all monoclinic, the space group being $P2_1/a$ (C_{2h}^5) in each case, and the two molecules in the unit cell each possess a center of symmetry. They are chosen to illustrate the type of result now being attained, but of course many other compounds, which cannot be discussed in detail in this article, have been extensively analyzed by the x-ray method. With relatively simple organic compounds, extremely accurate results have been obtained by Wyckoff (25, 26, 27) in his analysis of urea and thiourea. More recently, Wyckoff and Corey (27) have extended their measurements to hexa-

methylenetetramine, whose cubic symmetry is an uncommon feature of organic compounds. The early analysis of this compound by Dickinson and Raymond (9) was one of the first precise determinations of organic crystal structure. Among the more complicated structures, the work of Muller (17) on the long chain hydrocarbons is well known, and special reference should be made to the analysis of hexamethylbenzene and hexachlorobenzene by Lonsdale (14, 15), diphenyl and triphenyl by Dhar (7) and Pickett (19), chrysene by Iball (12), and to the recent work on cyanuric triazide by Knaggs (13). Convenient summaries of the work on a great many other organic compounds which have been studied, but usually without quantitative intensity measurements, will be found in the *Strukturbericht* of Ewald and Hermann (1931) and in a previous article by Hendricks.⁴

II. ANTHRACENE AND NAPHTHALENE

Figure 1 shows the final results of the Fourier analysis of anthracene (20) when the structure is projected along the direction of the *b*-axis. In this and all the other examples given below a two-dimensional Fourier series has been employed, following the method first used by W. L. Bragg (5), which gives a projection of the whole structure along a certain direction in the crystal. The structure in three dimensions can usually be built up by putting together the results of three or more projections of this kind. In the present examples only the projection which gives the most complete view of the individual molecule will be used, but it will be understood that the details of the structure have been worked out with the aid of the other projections.

Now, as we have seen, this contoured map of the electron distribution in anthracene is built up entirely from the experimental measurements of intensity, only the signs of the terms being taken from the trial structure; moreover, these signs are independent of the precise nature of the initial assumptions. The first thing to note is that the atoms are round where they are clearly resolved. Of course, the plane of the molecule is actually inclined at a high angle of over 60° to the plane on which the projection is drawn, so that certain pairs of atoms overlap in the picture and form unresolved ovals. The exact position of these atoms can usually be obtained from the other projections. Now atoms with spherical symmetry were assumed in the trial structure, but they were placed at points differing somewhat in position from those now found. The fact that the atoms, although shifted, remain round, is a confirmation of the whole analysis. If any considerable errors were involved, experimental or theoretical, there would be no particular reason for the atom remaining round.

⁴ See Chemical Reviews 7, 431 (1930).

The next thing we note about the structure is its regularity. The rows of atoms along the molecule, *B*, *D*, *F*, lie very accurately on parallel straight lines. Across the molecule, too, the lines joining pairs of atoms, *DD'*, *BF'*, are parallel. When the complete structure is worked out with the aid of the other projections it is found that the carbon rings are regular plane hexagons, the carbon to carbon distance being everywhere 1.41 A.U. This result is in harmony with our ideas of the chemical structure.

The chemist is, however, aware of another feature in the properties of anthracene. The 9, 10- or meso-positions on the middle ring are mark-

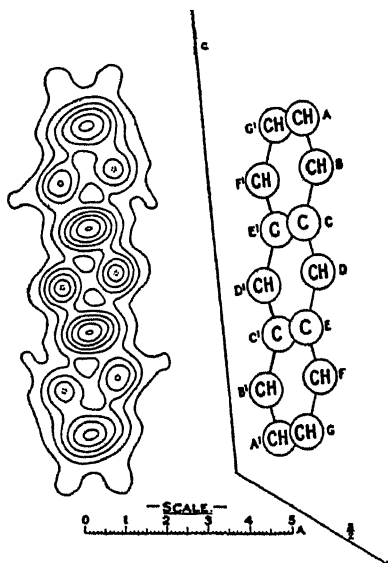


FIG. 1. Fourier projection map of the anthracene molecule, along the *b* crystal axis. Each contour line represents a density increment of 1.27 electrons per square Ångström unit. The dotted centers at *D* and *B* mark densities of just over seven and just under six electrons, respectively. The plane of the molecule makes an angle of about 62.4° with the plane of the projection.

This drawing and figures 2 to 14 are reproduced by permission of the Royal Society.

edly different in reactivity from the ordinary benz-positions of the end rings. Although carrying only one hydrogen atom, the meso-positions behave more like aliphatic than aromatic centers. Does the x-ray picture reveal any difference at these centers? As regards dimension there is no distortion of the structure at these points. The interatomic distances are the same as in the other rings. But there is a marked difference in the peak values of the electron density. On the meso-position it is about 7 electrons per square A.U., whereas on the benz-position it is only 5.5 to

6 electrons. The value seems to fall away as we pass outwards from the center of the molecule.

The meaning of this result is somewhat difficult to interpret. We must, of course, be cautious in accepting too fine detail in the picture. If the experimental measurements were made more accurate, and if still weaker reflections were included in the series, would the result persist? Probably it would, because it seems large enough to be real. But the density recorded on the atoms must depend in its absolute value very greatly on the temperature. Near the melting point all the values will be lower, owing to increase in the thermal movement, while at a lower temperature the peaks will be sharpened.

Further work has shown that a small falling-off in density at the end atoms seems to be a rather general effect in structures of this type, which are characterized by a very strong cleavage plane crossing the ends of the molecules. This cleavage plane corresponds to a large region of low or zero density in the projection. (Compare figure 3.) Now if we imagine an isolated carbon atom the F values applicable to organic compounds show that the electron density, instead of falling off abruptly to zero at the outside of the atom, tails away slowly, leaving a fringe around the atom,—an effect due partly to the temperature factor and partly to the outermost loosely bound electrons, which make little or no contribution to the x-ray reflection, and consequently appear in the Fourier synthesis as a more or less uniform background of density. Thus all the atoms inside the molecule are overlapped by their neighbors to a small extent, but those that border the large gap of the cleavage plane are overlapped like this on one side only. This is probably the explanation of the more general small falling-off in the peak values of the density of the outside or end atoms that is observed in the case of many compounds. But in anthracene the difference at the meso-atoms seems somewhat greater than can be explained in this way.

The molecules of naphthalene in the crystalline state display a very similar orientation to those of anthracene. Indeed, it was the striking similarity between the two crystals which attracted the attention of Sir William Bragg (3) in one of the earliest applications of the x-ray method to organic crystals. Figure 2 shows the Fourier projection map of naphthalene (21) which corresponds to the anthracene projection of figure 1. The dimensions of the rings are found to be the same as in anthracene, i.e., regular plane hexagons, with the carbon centres 1.41 A.U. apart. This repetition of the strictly planar structure, with the 1.41 A.U. inter-atomic distance, which emerges from an *entirely different set of experimental measurements*, is of great significance. It has long been known that in graphite (2) the atoms are arranged in sheets of condensed planar

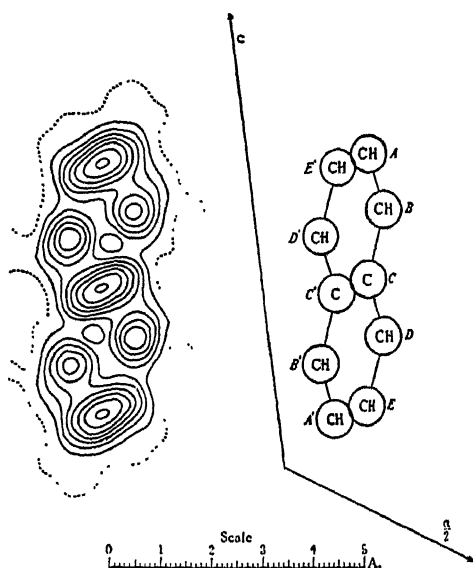


FIG. 2. Naphthalene projected along the b crystal axis. In this and all the subsequent maps each contour line represents a density increment of one electron per square Ångström unit, and the one electron line is dotted. The plane of the naphthalene molecule is here inclined to the plane of the projection at an angle of about 64.5° .



FIG. 3. A smaller scale projection of the naphthalene structure along the b crystal axis, showing how six molecules are built together in the crystal.

hexagons, the centers being 1.42 A.U. apart, and the distance between the layers being 3.41 A.U. In hexamethylbenzene also (14), where all the atoms reside on the basal plane of the crystal, similar relations hold. We now see that in complicated aromatic structures, where the molecules are inclined at various angles to all the crystal axes and planes, the molecule itself does not suffer any distortion, but remains a small *rigid* framework, held by the surrounding forces in some definite orientation.

In the naphthalene projection (figure 2) the peak values of the density are now all much more nearly equal than in anthracene, although there is a small falling-off at the end atoms when the structure is projected along the *a* crystal axes. Figure 3 shows the projection on a smaller scale, and illustrates how a group of six molecules is built together in the crystal. The strong (001) cleavage plane passes across the ends of the molecules, through a region of very low electron density. It should be noted that in this diagram (and in figure 5) the central molecule in each row is the same as the others. This is only true, however, of this particular direction of projection, viz. along the *b*-axis. The central molecule is actually half a translation along the *b*-axis, out of the plane of the paper, and it is also inclined to the plane of the paper in the opposite sense to that of the end molecules. In other words, it is derived from the end molecule by a reflection in the plane of the paper, or by a rotation of 180° about the *b*-axis. The side atoms of the molecules are thus not actually as close as they appear in this projection.

III. DURENE AND BENZOQUINONE

As we have now determined the form of the molecule in these fused ring aromatic compounds, let us pass on to the consideration of some substituted benzene derivatives, when the variety of the chemical reactions is larger and many interesting problems present themselves. Symmetrical tetramethylbenzene (durene) is suitable for a detailed analysis (22), and the Fourier projection along the *b*-axis is shown in figure 4. In this case all the atoms in the molecule are separately resolved. The measurements which have been made show again that the benzene ring is a regular plane hexagon structure of dimensions similar to those obtained for naphthalene and anthracene, although the inclination of the molecule to the plane of the drawing causes a large apparent distortion. Figure 5 shows on a smaller scale how a group of molecules is arranged in the crystal.

The chief interest in this structure perhaps lies in the situation of the methyl groups. If the substitution were entirely symmetrical, the three valencies of the carbon atom would make angles of 120° with each other. Careful measurement shows, however, that this is not exactly the case. There is a small, but apparently definite displacement of the methyl

groups away from each other towards the unsubstituted positions of the ring. Figure 6 shows the actual dimensions of the molecule worked out from this and other projections. The displacement of the methyl groups

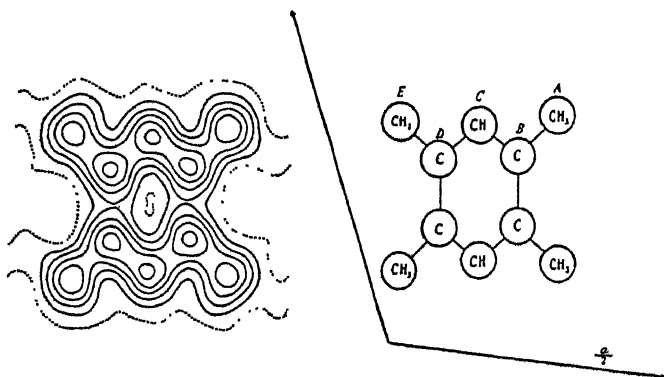


FIG. 4. Durene (*sym*-tetramethylbenzene) projected along the *b* crystal axis. The plane of the molecule is inclined at an angle of about 48.6° to the plane of the projection, causing a large apparent distortion in the shape of the hexagonal benzene ring. The methyl groups suffer a small but apparently true displacement away from each other towards the unsubstituted position.

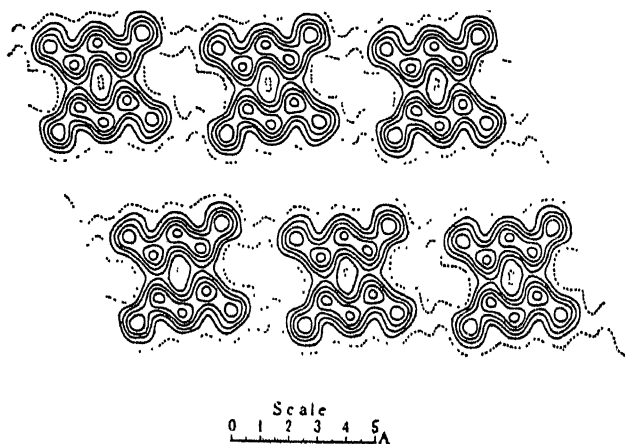


FIG. 5. A small scale map of the durene structure. Note the large gap of low density along the cleavage plane.

is seen to be only 3° , but there is no doubt that this figure would increase if more bulky groups were substituted. By extending the work to other examples we may hope to approach the problems of stereochemistry in a quantitative manner.

The main result of the work we have illustrated so far has been to show that the benzene ring, whether in condensed ring systems or in a simple substituted benzene derivative, is an apparently rigid structure in the form of a regular plane hexagon. The carbon to carbon distance, equal to the "radius" of the ring, has the very constant value of 1.41 A.U. The radius of the ordinary tetrahedral carbon atom as in diamond is 1.54 A.U., so that we have here a new kind of tervalent atom of smaller size, with three coplanar valencies making angles of 120° with each other. We have no evidence of the alternating double and single bonds of the Kekulé formula, but of course we should not expect to be able to find these, because the essential feature of the Kekulé formula is that the double and single bonds are supposed to be continually changing position, or to be otherwise in equilibrium, in a manner which makes all six corners of the ring equivalent. Our results are in accord with the modern conception of a ring in which the links are of intermediate character between the double and single

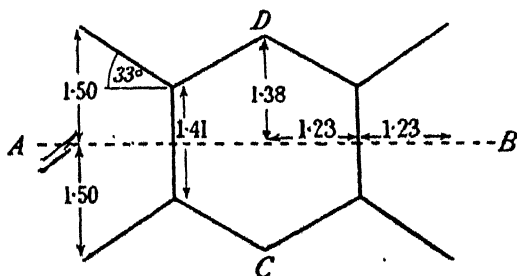


FIG. 6. Dimensions of the durene molecule obtained from the complete structure determination.

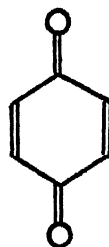


FIG. 7. Benzoquinone

bond. Now if we examine a compound in which the "double bonds" of the ring have been stabilized, for example, by the introduction of divalent groups, then it might be possible to detect some distortion in the dimensions of the ring caused by contraction at the double bonds and alteration of the valency angles.

This has actually been carried out in the case of benzoquinone (24). The compound carries two oxygen atoms in the *p*-positions, so that there is now only one way in which the ring bonds can be arranged (disregarding the "peroxide" formula, which seems rather improbable and is, in fact, definitely ruled out by the following work). The chemistry of the compound supports this formulation, as bromine, etc., can be taken up at the double bonds (cf. figure 7).

The x-ray analysis of this compound shows that the molecular planes are nearly parallel, but unfortunately the molecules are found to interleave one another in a manner which makes it difficult to obtain a clear two-

dimensional Fourier projection. In the trial structure a regular benzene ring was assumed, so it is of interest to see if any deviation from this regularity is brought to light by means of the Fourier analysis. The best projection that can be obtained is shown in figure 8, where the molecules are viewed at a fairly high angle. It will be seen that the two oxygen atoms and two of the carbon atoms are clearly resolved, but the precise position of the other carbon atoms is obscure. The other projections yield even less definite information.

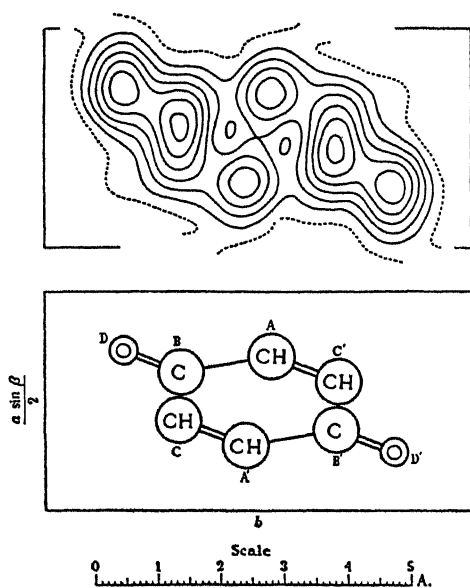


FIG. 8. Benzoquinone projected along the c crystal axis. The high inclination of the plane of the molecule to the plane of the projection (about 59.5°) makes the resolution of certain atoms difficult.

Closer inspection of this diagram, however, at once reveals a departure from regularity in the form of the ring. In a regular plane hexagon opposite sides are parallel to each other and to the line through the center joining the other two corners (cf. figure 9), and these lines will remain parallel in any projection of the structure. Now although the precise position of the overlapping side pairs of carbon atoms is obscure, it can be seen that the line on which they lie is definitely not parallel to the line through the center of the ring joining the other two carbon atoms. The effect, however, is not very reliable, because of the influence of the adjoining atoms whose overlap will tend to pull the line round in any case.

In order to get a fair comparison the central ring in anthracene, which happens to display a closely similar orientation in the crystal, has been isolated, and is shown in the upper part of figure 10. Now we know from other projections that the anthracene ring is very exactly a regular plane hexagon. And although the influence of adjoining atoms is here very similar to what it is in benzoquinone, it can be seen that the ovals now remain reasonably parallel in general direction to the line through the center. The lower part of the figure shows the benzoquinone projection, and the convergence of the lines is pronounced.

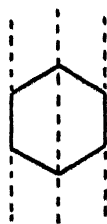


FIG. 9. Regular hexagon

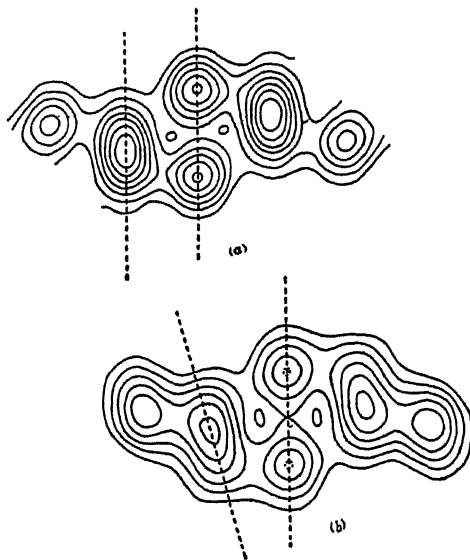


FIG. 10. The central ring of anthracene (a) compared with the carbon ring in benzoquinone (b).

Apart from the distortion of the ring, the carbon to oxygen distance is of interest in the compound. This cannot be measured very directly because the carbon atom to which the oxygen is directly attached remains obscured in all the projections. We can, however, measure quite accurately the distance between the oxygen and the carbon one place removed round the ring, and also the distance between the two oxygen atoms. From these measurements we can work out the direct carbon to oxygen distance. If a regular benzene ring is assumed the distance obtained is 1.31 A.U., but if allowance is made for the distorted ring, the carbon to oxygen distance is only 1.14 A.U.

The band spectrum analysis of carbon dioxide (1) gives the carbon

oxygen distance as 1.15 A.U. (The results from attempts at the crystal analysis of solid carbon dioxide are rather variable.) In urea (11, 25, 27) the crystal results are consistent with a somewhat higher value for the carbon to oxygen distance of 1.25 A.U. The ketonic oxygen in benzoquinone is thus seen to be rather similar to the oxygen in carbon dioxide if the distorted ring is correct.

The molecular model which gives the best explanation of all the Fourier projections of the benzoquinone structure is illustrated in figure 11. (It will be noticed that the convergence of the dotted lines is not so pronounced now as it was when the molecule was viewed at a high angle in figures 8 and 10.) Carbon atoms connected by a double bond are 1.32 A.U. apart, and those connected by a single bond are at the greater distance of 1.50 A.U., while the angle between the single bonds has the tetrahedral value of $109\frac{1}{2}^\circ$, and between the double and the single bonds 125° . Owing to the peculiarities of this structure the results are not so clear cut

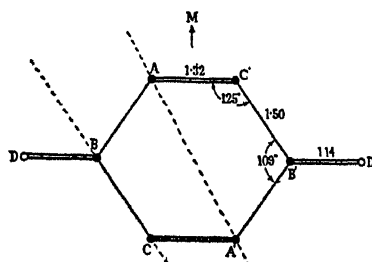


FIG. 11. Dimensions of the benzoquinone molecule

and definite as they were, for example, in durene and anthracene. An alteration of a few degrees or a few hundredths of an A.U. in these figures would not have much effect on the projections. But the general conclusion is that the x-ray evidence is rather definitely in favor of the distorted ring, as opposed to the regular benzene ring.

IV. DIBENZYL

The x-ray analysis of one further compound will be considered, because it introduces a type of problem which we have not come across in the previous examples, viz., that arising from the possibility of free rotation of groups about a single bond. In durene the $-\text{CH}_3$ groups are attached to the benzene nucleus by a single bond, but as the hydrogen atoms have an almost inappreciable effect on the x-ray scattering, we cannot make any very reliable observations of their position. But in dibenzyl (23) we have two benzene rings connected by two $-\text{CH}_2$ groups, and free rotation

should be possible about the bonds between the rings and the $-\text{CH}_2$ groups, and between the $-\text{CH}_2$ groups themselves, so that the molecule as a whole has several degrees of freedom. The symmetry of the structure tells us at once that in the crystal the benzene rings are parallel and oriented in the same way, because the molecule contains a center of symmetry. There remains the problem of finding the orientation of the molecule in the crystal, and also its exact shape, i.e., whether the benzene rings are coplanar, or whether though parallel they lie in different planes. Two possibilities are illustrated in figures 12 and 13.

The result of the x-ray analysis shows that the benzene rings do lie in different planes, and that these are in fact almost perpendicular to the plane containing the zigzag of the connecting $-\text{CH}_2$ groups, as shown in figure 13. The projection of the structure along the b -axis, obtained by Fourier analysis, is shown in figure 14. We see that the benzene rings are apparently quite regular. The connecting $-\text{CH}_2$ groups are separately resolved, so that their position can be estimated with some accuracy.

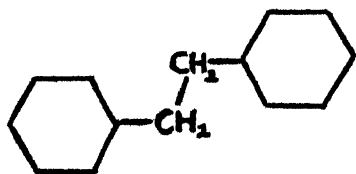


FIG. 12. Dibenzyl, planar molecule

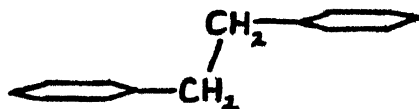


FIG. 13. Dibenzyl, three-dimensional molecule

In a complicated structure like this, however, it is very necessary to study the other projections as well, in order to build up a complete three-dimensional picture of the molecules.

The final results show that the benzene rings are of the usual regular hexagon type, that the connecting $-\text{CH}_2$ groups are situated at 1.47 A.U. from the aromatic carbon, and that the distance between the CH_2 groups is 1.58 A.U. (This latter figure is a little uncertain. The overlapping effect of the hydrogen atoms may account for the deviation from the diamond value of 1.54 A.U.) The angle of the $-\text{CH}_2-\text{CH}_2-$ zigzag works out at 111° , which is as near to the tetrahedral value as we can expect, considering the experimental uncertainties. The planes of the rings do not appear to be strictly perpendicular to the plane of the $-\text{CH}_2-\text{CH}_2-$ zigzag, being apparently turned round by about 16° . The nature of the projection makes it difficult to be quite sure of this distortion from regularity. Although the figure seems large enough to be significant, it only means that the planes of the rings are some 4 per cent closer together than they would be in a perfectly regular model.

It is most likely that in the liquid or gaseous states free rotation can take place about the single bonds in this compound, and that in the crystal the molecule assumes this particular form because it is best adapted to the van de Waals forces. The chemical evidence of free rotation lies in the fact that there is only one compound known, and not two distinct compounds as in stilbene, where a double bond unites the groups. In dibenzyl, if the molecule had only one stable configuration, it would seem to account for the known facts just as well as the conception of all possible configurations being equally favored. This question might have bearings

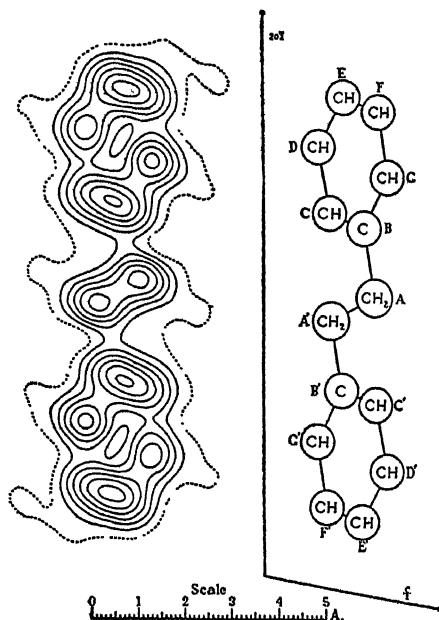


FIG. 14. Dibenzyl projected along the *b* crystal axis. The benzene rings lie in parallel planes, about 1.42 Å. U. apart, and inclined to the plane of the drawing at about 58.8° .

of chemical interest, and could probably be tested by x-ray or electron diffraction experiments on the vapor of the compound.

It is of interest to note that in discovering the arrangement of the atoms in the dibenzyl molecule we have had to go considerably beyond the information contained in the chemical formula, which, of course, says nothing about the *absolute* position of the rings with respect to the $-\text{CH}_2$ groups. We are thus led to consider the possibility of quantitative analysis of organic compounds whose structure has not been fully determined by chemical methods. If very little is known about the structure chemically,

then it would still appear rather hopeless to attempt the problem by means of x-ray analysis. But if the main outlines of the structure have been determined by chemical means, then it does not seem impossible that the remaining detail might be fixed by x-ray analysis. The difficulty in practice is that the organic problems which it would be most interesting to attempt to solve in this manner usually involve molecules containing a very large number of atoms, compared to the number in those simple structures we have been considering. This complication enormously increases the labor of the analysis. But by improvement in technique, and by studying the social habits of the molecules in the simpler crystals which have so far yielded to analysis, we may in time gain enough experience to make a reasonable attempt in this direction.

V. CONCLUSION. SUMMARY OF INTERATOMIC DISTANCES

In the preceding pages we have dealt with those organic structures which have, up to the present time, been most intensively analyzed by the x-ray method. The results obtained illustrate the great power and beauty of this method of investigating problems of molecular structure in the solid state. Perhaps the most striking feature of the results is the amazing verification which they afford of the stereochemical conceptions of organic chemistry. Of course it may be argued that these fundamental formulas did not stand in any need of verification—they were firmly established by chemical methods long before the diffraction of x-rays was discovered, indeed before the discovery of x-rays at all. But the experimental methods employed in building up the molecular maps which illustrate this paper are so remote from the reactions and syntheses which establish the chemical structural formulas, that the verification afforded is of considerable philosophical interest. The structural formulas are now endowed with a new degree of reality—not necessarily more profound, but certainly quite a different reality.

The greatest difference lies in the exact metrical representation of the structures which has now been achieved. The interatomic distances appear as constants which are definitely characteristic of certain types of binding between the atoms. These constants can be related to the heats of formation and other physical properties, and furnish data for theoretical investigation. The minimum intermolecular distances between certain groups belonging to adjoining molecules in the crystal are also characteristic constants which must prove of importance in the quantitative study of reactions.

Many other organic compounds besides those dealt with in the preceding pages have been investigated by the x-ray method, with varying degrees of success and completeness. These are included in a table of interatomic

TABLE 1
Atomic distances in organic compounds by x-ray analysis

COMPOUND	INTRAMOLECULAR DISTANCE IN Å.	MINIMUM INTERMOLECULAR DISTANCE IN Å.	TYPE OF STRUCTURE AND ANALYSIS	REFERENCE
Diamond.....	C—C 1.541		Cubic	(4, 10)
Graphite.....	C—C 1.42	C ... C (between layers) 3.41	Hexagonal layer structure	(2)
Hexamethylbenzene.....	C—C aromatic 1.42 C—CH ₃ aromatic-aliphatic 1.48		Triclinic layer structure (trial analysis)	(14)
Cyanuric triazine.....	C—N in ring 1.38 C=N in ring 1.31 C—N outside ring ~1.38 N≡N terminal 1.11 N=N 1.26	N ... N 3.12	Hexagonal layer structure (One Fourier projection)	(13)
Nonacosane.....	CH ₂ —CH ₂ , aliphatic 1.553*	CH ₂ ... CH ₂ 3.6-3.9	Linear structure	(17)
Hydrocarbon series C _n H _{2n+2}	CH ₂ —CH ₂ , aliphatic 1.534*		Linear structures	(18)
Anthracene.....	C—C aromatic 1.41	CH ... CH 3.7	Three Fourier projections	(20)
Naphthalene.....	C—C aromatic 1.41	CH ... CH 3.6	Three Fourier projections	(21)
Durene.....	C—C aromatic 1.41 C—CH ₃ , aromatic-aliphatic 1.47	CH ₃ ... CH ₃ 3.9	Three Fourier projections	(22)
Dibenzyl.....	C—C aromatic 1.41 CH ₂ —CH ₂ , aliphatic 1.58 C—CH ₃ , aromatic-aliphatic 1.47	CH ₂ ... CH 4.1 CH ... CH 3.7	Three Fourier projections	(23)

Benzoquinone.....	C—C in ring C=C in ring C=O	~1.50 ~1.32 ~1.14	C ... CH C ... O O ... O	3.45 3.36 3.62	Three Fourier projections	(24)
Chrysene.....	C—C aromatic	1.41	CH ... CH	3.4	One Fourier projection	(12)
<i>p</i> -Diphenylbenzene.....	C—C aromatic C—C between rings	1.42 1.48	CH ... CH	3.9	One Fourier projection	(19)
Hexachlorobenzene.....	C—Cl	> 1.79			One Fourier projection	(15)
Urea.....	C—NH ₂ C=O	1.37 1.25	NH ₂ ... O	3.2	One Fourier projection (tetragonal)	(11, 25, 27)
Thiourea.....	C—NH ₂ C=S	1.35 1.64	NH ₂ ... NH ₂ NH ₂ ... S	3.8 3.4	One Fourier projection	(26)
Hexamethylenetetra- mine.....	CH ₂ —N	1.42			One Fourier projection (cubic)	(9, 27)
<i>β</i> -Benzene hexabromide..	CH—Br	1.94†	Br ... Br	3.74	Trial analysis (cubic)	(8)
<i>β</i> -Benzene hexachloride.	CH—Cl	1.81†	Cl ... Cl	3.59	Trial analysis (cubic)	(8)
Diphenyl.....	C—C aromatic C—C between rings	1.42 1.48			Trial analysis	(7)
Oxalic acid dihydrate....	C—C aliphatic C—O oxalate	1.59 1.25	O ... O oxalate O ... H ₂ O	3.21 2.60	Trial analysis	(28)

* Assuming tetrahedral angle.

† Assuming tetrahedral cyclohexane ring.

and intermolecular distances (table 1), which forms a convenient summary of this review. Generally it is only in the case of carbon itself and a few specially simple structures that the measurement of interatomic distance can be carried out in anything like a straightforward manner. In the vast majority of organic crystals the structures are very complex and of low symmetry. The number of variables is so great that estimates of interatomic distance made by trial and error analysis in these cases are often unreliable. But when accurate intensity measurements are made, and the results are refined by the application of intensive Fourier analysis, as in the examples dealt with in this paper, then the estimate of interatomic distance obtained really amounts to a direct measurement. This kind of exhaustive analysis is very difficult and laborious, but it is the only kind of real value in dealing with complex organic molecules. As some guidance to the weight to be attached to the data in the following table, the type of analysis is indicated. In a few structures the atoms all reside on some simple crystal plane (layer structures), or in rows along some axis (linear structures). In these cases a less exhaustive analysis can yield accurate results. But they are exceptions. In the vast majority of organic crystals the orientations of the molecules do not bear a simple relation to the crystal axes.

The table might be extended by the inclusion of many other compounds which have been analyzed by the method of trial and error only. But unless such structures have some simplifying feature, the estimates of interatomic distances are not likely to be very reliable, and so results of this kind have in general been omitted.

REFERENCES

- (1) BARKER, E. F., AND ADEL, A.: *Phys. Rev.* **44**, 185 (1933).
- (2) BERNAL, J. D.: *Proc. Roy. Soc. London* **106A**, 749 (1924).
- (3) BRAGG, W. H.: *Proc. Phys. Soc. London* **34**, 33 (1921).
- (4) BRAGG, W. H., AND BRAGG, W. L.: *Proc. Roy. Soc. London* **89A**, 277 (1913).
- (5) BRAGG, W. L.: *Proc. Roy. Soc. London* **123A**, 537 (1929).
- (6) BRAGG, W. L., AND WEST, J.: *Phil. Mag.* **10**, 823 (1930).
- (7) DHAR, J.: *Indian J. Physics* **7**, 43 (1932).
- (8) DICKINSON, R. G., AND BILICKE: *J. Am. Chem. Soc.*, **50**, 764 (1928).
- (9) DICKINSON, R. G., AND RAYMOND, A. L.: *J. Am. Chem. Soc.* **45**, 22 (1923).
- (10) EHRENBERG, W.: *Z. Krist.* **63**, 320 (1926).
- (11) HENDRICKS, S. B.: *J. Am. Chem. Soc.* **50**, 2455 (1928).
- (12) IBALL, J.: *Proc. Roy. Soc. London* **146A**, 140 (1934).
- (13) KNAGGS, I. E.: *Nature* **135**, 268 (1935); *Proc. Roy. Soc. London A* (1935), in press.
- (14) LONSDALE, K.: *Proc. Roy. Soc. London* **123A**, 494 (1929).
- (15) LONSDALE, K.: *Proc. Roy. Soc. London* **133A**, 536 (1931).
- (16) MARTIN, P. E., AND BARKER, E. F.: *Phys. Rev.* **41**, 291 (1932).
- (17) MULLER, A.: *Proc. Roy. Soc. London* **120A**, 437 (1928).

- (18) MULLER, A.: Private communication.
- (19) PICKETT, L. W.: Proc. Roy. Soc. London **142A**, 333 (1933).
- (20) ROBERTSON, J. M.: Proc. Roy. Soc. London **140A**, 79 (1933).
- (21) ROBERTSON, J. M.: Proc. Roy. Soc. London **142A**, 674 (1933).
- (22) ROBERTSON, J. M.: Proc. Roy. Soc. London, **141A**, 594 (1933); **142A**, 559 (1933).
- (23) ROBERTSON, J. M.: Proc. Roy. Soc. London **146A**, 473 (1934); also paper in press (1935).
- (24) ROBERTSON, J. M.: Nature **134**, 138 (1934); Proc. Roy. Soc. London A (1935), in press.
- (25) WYCKOFF, R. W. G.: Z. Krist. **81**, 102 (1932).
- (26) WYCKOFF, R. W. G., AND COREY, R. B.: Z. Krist. **81**, 386 (1932).
- (27) WYCKOFF, R. W. G., AND COREY, R. B.: Z. Krist. **89**, 462 (1934).
- (28) ZACHARIASEN, W. H.: Z. Krist. **89**, 442 (1934).

THE CHLOROVINYLSARSINES

KIRBY E. JACKSON AND MARGARET A. JACKSON

Department of Chemistry, Vanderbilt University, Nashville, Tennessee

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Following the announcement by Gibson and Pope (10) that ethylene is absorbed by the chlorides of sulfur, forming β, β' -dichlorodiethyl sulfide, Green and Price (12) began their study of the action of acetylene and ethylene upon inorganic, anhydrous chlorides.

Dafert (4) studied the reaction of acetylene upon arsenic trichloride at ordinary temperature and at the boiling point of the latter and found that there was no appreciable reaction; in the presence of anhydrous aluminum chloride at ordinary temperature, however, he isolated a product, a heavy, yellow oil, boiling at 108°C. at 7 mm. and at 250°C. at 760 mm., specific gravity, d_4^{15} , 1.6910, with strongly irritating vapors but not marked by poisonous properties although exhibiting strong bactericidal power, to which he gave the name diacetylene arsenic trichloride and ascribed the formula, $\text{AsCl}_3 \cdot 2\text{C}_2\text{H}_2$. He apparently regarded the substance as an association product rather than a secondary arsine, although the properties correspond to those of bis(β -chlorovinyl)chloroarsine. He does not report finding the corresponding compounds of arsenic trichloride with one and three molecules of acetylene, respectively.

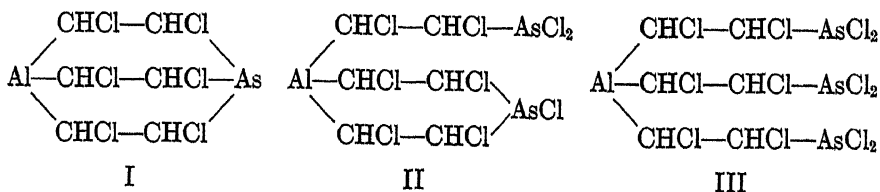
Lewis and Stiegler (18) likewise found that all efforts to add acetylene to arsenic trichloride directly under a wide variety of physical conditions proved ineffectual. After many catalysts employed, only two, aluminum chloride and mercuric chloride, have served to effect the addition. The addition of acetylene to arsenic trichloride, both with and without polymerization, is recorded by Baud (2), and a number of compounds of aluminum chloride, acetylene, and alcohol have been isolated by Gangloff and Henderson (7). Fischer (6) added arsenic trichloride to the acids of the acetylene series, and found that the addition of arsenic trichloride and chlorine took place at the triple bond.

As to the use of aluminum chloride in this reaction, it was shown by Lewis and Perkins (17) and confirmed by Mann and Pope (19) and Green and Price (12) that an intermediate addition compound is formed of one molecule each of arsenic trichloride and aluminum chloride with three molecules of acetylene, $\text{Al}(\text{CHClCHCl})_3\text{As}$. This conclusion was based

upon the observation that a fresh reaction mixture on processing yields more tris(β -chlorovinyl)arsine, $(\text{ClCH}:\text{CH})_3\text{As}$, than is present in an equilibrium mixture of arsenic trichloride, β -chlorovinylchloroarsine, bis(β -chlorovinyl)arsine, and tris(β -chlorovinyl)arsine, of the same acetylene content. In other words, some agency had caused more molecules of acetylene to combine with arsenic in the ratio of three of acetylene to one of arsenic than is found under equilibrium conditions. This equilibrium value was previously established by heating pure tris(β -chlorovinyl)arsine with arsenic trichloride until the system had reached a constant value for the four components present.

Moreover it was found noteworthy, that when a fresh reaction mixture of arsenic trichloride, aluminum chloride, and acetylene was allowed to stand at room temperature, or preferably warmed in the presence of free arsenic trichloride, there was an appreciable rise in the content of the primary and secondary chlorovinylarsines at the expense of the tertiary. This shift of the system in favor of the primary and secondary arsines could be increased by the addition to the fresh reaction mixture of more arsenic trichloride, before it had been allowed to stand or become warmed. Curiously enough, a number of substances, particularly metallic aluminum, increased the velocity of the change to equilibrium.

It was concluded, therefore, that the three arsines had their origin in the three following intermediate compounds:



Compound I was believed by Lewis and Stiegler (18) to be formed when acetylene is conducted into arsenic trichloride containing aluminum chloride; compounds II and III are formed by the further reaction of compound I with one and two more molecules, respectively, of arsenic trichloride.

The arsines are obtained from these intermediate compounds by washing the reaction mixture with 20 per cent hydrochloric acid to constant volume and distilling the resulting mixture. The intermediate compounds undergo hydrolysis, the aluminum being removed in the dilute hydrochloric acid.

Further experimental evidence in support of this explanation of the reaction was sought on the following basis. Three molecules of acetylene may add one molecule each of arsenic trichloride and aluminum chloride simultaneously, or in two steps. Presumably, the addition takes place in two steps, the aluminum chloride adding first to form $(\text{CHCl}:\text{CH})_3\text{Al}$,

since acetylene cannot be made to add arsenic trichloride in the absence of a suitable catalyst. Moreover, aluminum chloride is known to add acetylene. This intermediate catalyst compound would then add arsenic trichloride to form the assumed parent compound, $\text{Al}(\text{CHClCHCl})_3\text{As}$. It may be seen at once that if this assumption is correct the halogens on the original arsenic and aluminum, respectively, are attached to the carbon atoms in the β -position to the corresponding metal. On hydrolysis, distilling, etc., the aluminum chloride and the organic arsenic compounds would be freed with the same halogen atoms as those with which the respective metals were originally combined. Therefore, the nature of the halide of arsenic used in the reaction determines the nature of the halogen in the resulting organic arsenical compounds, irrespective of the kind of aluminum halide used as the catalyst. Arsenic trichloride should give a vinylarsine containing chlorine, and arsenic tribromide a compound containing bromine with either aluminum chloride or aluminum bromide. Arsenic tribromide, acetylene, and aluminum chloride would thus form $\text{Al}(\text{CHBrCHCl})_3\text{As}$ as an intermediate compound, while arsenic trichloride and aluminum bromide should simultaneously give $\text{Al}(\text{CHClCHBr})_3\text{As}$. The former would finally yield bromoarsines and the latter chloroarsines.

This has been found by Mann and Pope (19) to be experimentally true and offers further experimental confirmation of this explanation of the reaction. Moreover, in no instance were organic arsenic compounds isolated containing mixed halogens.

β -CHLOROVINYLDICHLOROARSINE, CHCl:CHAsCl_2

The most important chlorovinylarsine, the chemical agent which created the most discussion during the latter part of the World War and about which many unauthentic stories were circulated, was "Lewisite," or, as the press and laity called it, "Methyl," chemically known as β -chlorovinyl-dichloroarsine and having the formula represented by CHCl:CHAsCl_2 .

Preparation

β -Chlorovinyl-dichloroarsine has been prepared, along with the secondary and tertiary arsines, by passing acetylene into arsenic trichloride to which has been added anhydrous aluminum chloride (9, 12, 17, 18, 19, 21); by reducing a hot hydrochloric acid solution of β -chlorovinylarsinic acid, $\text{CHCl:CH—AsO}(\text{OH})_2$, with sulfur dioxide using hydrogen iodide as a catalyst (9); by heating a mixture of arsenic trichloride with tris(β -chlorovinyl)arsine in a sealed tube for four hours at 220°C . according to the reaction (12):



Physical properties

β -Chlorovinyl-dichloroarsine is a colorless or faintly yellow liquid miscible in all proportions with absolute alcohol, benzene, kerosene, olive oil, liquid petrolatum, and the common organic solvents. It is insoluble in cold water or dilute acids, but is hydrolyzed on standing or warming in water. It is colorless and stable when pure, but in the presence of small amounts of arsenic trichloride acquires a violet to dark purple color on standing, the speed of the change and the depth of color depending upon the amount of arsenic trichloride present as an impurity (17).

It has the following physical constants. Boiling point: 203°C. (14), 190°C. (1, 17, 26, 28), 98°C. at 30 mm. (17), 96°C. at 30 mm. (12), 93–94°C. at 24 mm. (3), 93°C. at 26 mm. (12), 82°C. at 16.5 mm. (19), 79°C. at 15 mm. (17), 77–78°C. at 12 mm. (29), 76.1°C. at 10 mm. (9), 76–77°C. at 12.5 mm. (19), 72°C. at 10 mm. (17), 71–74°C. at 15 mm. (27), 69.5–70.5°C. at 10 mm. (13). Its melting point has been reported as follows: 0.1°C. (9, 15), –13°C. (1, 26, 28). Specific gravity: $d_{4.0}^{10.6}$, 1.8954 (13); $d_{4.0}^{20}$, 1.8880 (17); $d_{4.0}^{23.7}$ (vacuum), 1.8819 (15); $d_{4.0}^{26.1}$ (vacuum), 1.8754 (9); $d_{4.0}^{30}$ (vacuum), 1.8648 (9). Vapor pressure, $\log = 9.123 - 2781.69/T$ (17); 0.087 at 0°C. (28); 0.395 at 20°C. (28). One cubic meter of saturated vapor contains 0.395 g. at 20°C., 15.60 g. at 40°C. (1, 26, 28). The index of refraction at 10.6°C. has the following values: $n_a = 1.6092$, $n_D = 1.6153$, $n_B = 1.6333$ (13); at 23.7°C., $n_C = 1.6025$, $n_D = 1.6092$, $n_F = 1.6251$ (15). The molecular refraction for the D sodium line is 38.14 at 10.6°C. (13), 38.16 at 23.7°C. (15); for the α and β hydrogen lines at 10.6°C., it is 37.83 and 38.98, respectively (13).

Chemical properties

(a) *Reaction with water.* When an alcoholic solution of β -chlorovinyl-dichloroarsine is added to water, complete hydrolysis of the chlorine attached to the arsenic occurs within a few minutes at 20°C.; at 5°C., 90 per cent hydrolyzes rapidly, the rest more slowly; undiluted at 20°C., it hydrolyzes similarly to the alcoholic solution at 5°C. (22).

(b) *Reaction with an alkali hydroxide.* A dilute solution of an alkali hydroxide, even when cold, causes a vigorous reaction, acetylene being evolved with brisk effervescence which is quantitative, according to Nekrasov and Nekrasov (21). When β -chlorovinyl-dichloroarsine is treated with one-half its weight of water and an excess of dilute ammonium hydroxide is added slowly, β -chlorovinylarsenious oxide, CHCl:CHAs:O , is formed. It is a white crystalline powder melting at 143°C. when slowly heated; it is very slightly soluble in water and carbon disulfide, more soluble in xylene and slightly soluble in alcohol, especially when boiled (18).

(c) *Reaction with halogens.* Halogens are rapidly absorbed with the formation of a variety of products. Thus, if a dilute solution of bromine in carbon tetrachloride be added slowly to a solution of the chloroarsine in the same solvent, the color of the bromine slowly disappears, and on shaking, or on keeping, fine leaflets of a bromo compound separate, m.p. 122°C. (12).

(d) *Reaction with nitric acid.* β -Chlorovinylidichloroarsine is vigorously oxidized when warmed with an equal volume of concentrated nitric acid; the oxidation sets in spontaneously in the cold, and the resulting solution, when chilled and scratched, deposits β -chlorovinylarsinic acid, CHCl:CHAsO(OH)_2 , as a mass of colorless crystals. The acid crystallizes from a mixture of acetone and carbon tetrachloride in long needles, melting at 130°C. (19). When crystallized from organic solvents such as an equal mixture of acetone and carbon tetrachloride, the crystals appear as fine needles. Both these latter and the larger, flat, hexagonal type obtained by the action of hydrogen peroxide on β -chlorovinylarsenious oxide show the same crystallographic measurements and characteristics. Both kinds of crystals are biaxial, positive, orthorhombic, and have the same measurements: α , 1.555; β , 1.565; γ , 1.705; birefringence $\gamma - \alpha$, 150 (18). When the acid is heated in a vacuum at 110–115°C., it loses one molecular proportion of water, giving the corresponding anhydride, β -chlorovinylarsenic oxide, CHCl:CHAsO_2 . It forms a fine, white hygroscopic powder and decomposes violently at 242°C. All attempts to recrystallize it result in the production of the original acid (19).

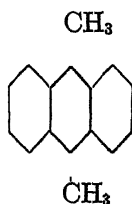
(e) *Reaction with hydrogen sulfide.* β -Chlorovinylarsenious sulfide, CHCl:CHAs:S , has been prepared by Mann and Pope (19), Lewis and Stiegler (18), and Kretov and Berlin (16) by passing hydrogen sulfide into an absolute alcohol or carbon tetrachloride solution of β -chlorovinylidichloroarsine. Neither Mann and Pope (19) nor Lewis and Stiegler (18) were able to effect a crystallization of the sulfide, obtaining a pale yellow, viscous liquid with a strong garlic-like odor; the liquid solidified to a hard resin on strong cooling. Kretov and Berlin (16), however, by bringing the mixture to a boil and then quickly cooling it, are said to have obtained light yellow plates with a repulsive odor, soluble in carbon disulfide and chloroform, slightly soluble in alcohol.

(f) *Reaction with potassium iodide.* Upon adding a concentrated hydrochloric acid (density 1.5) solution of potassium iodide to β -chlorovinylidichloroarsine there is formed β -chlorovinylidiiodoarsine, CHCl:CHAsI_2 , yellowish-brown crystals, melting at 37.5–38.5°C., somewhat soluble in ligroin and very soluble in alcohol and benzene (18).

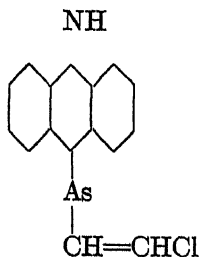
(g) *Reaction with potassium thiocyanate.* On treating a hot alcoholic solution of potassium thiocyanate with an absolute alcoholic solution of

β -chlorovinyl-dichloroarsine, Lewis and Stiegler (18) obtained β -chlorovinylhydroxythiocynoarsine, CHCl:CHAs(OH)CNS , an oil, soluble in water but unstable in air.

(h) *Reaction with benzene.* When β -chlorovinyl-dichloroarsine is allowed to react with benzene in the presence of anhydrous aluminum chloride there is formed 9, 10-dimethylantracene, m.p. 180–181°C. (9).

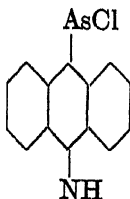


(i) *Reaction with diphenylamine.* (1) When a mixture of β -chlorovinyl-dichloroarsine and diphenylamine is heated gently, hydrogen chloride fumes are freely evolved and on cooling a thick mass of green crystals of 6- β -chlorovinylphenarsazine



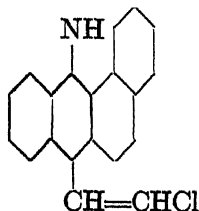
is formed. The compound is soluble in hot xylene, in acetone-carbon tetrachloride mixture, and in absolute alcohol; it is insoluble in ether. It melts at 186–187°C. It is decidedly irritating to the eyes and nostrils (18).

(2) 10-Chloro-5,10-dihydrophenarsazine,



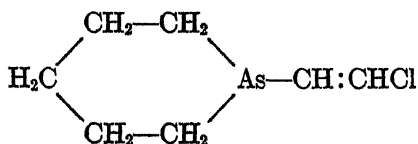
is prepared by boiling a mixture of diphenylamine, β -chlorovinyl-dichloroarsine, and *o*-dichlorobenzene under a reflux for twelve hours (3, 25). It boils at 120–121°C. at 9–10 mm.; its specific gravity, d_{20}^{20} , is 1.6766 (25).

(j) *Reaction with phenyl- α -naphthylamine.* Upon adding phenyl- α -naphthylamine to β -chlorovinyl-dichloroarsine there separate the well-defined, bright yellow, needle-like crystals of 7- β -chlorovinyl-7, 12-dihydro- γ -benzophenarsazine.



The melting point of the compound has been given as 213°C. (18) and as 218–220°C. (3).

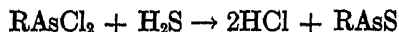
(k) *Reaction with α, ϵ -dichloropropane.* Cyclopentamethylene- β -chlorovinylarsine,



is prepared by treating magnesium with α, ϵ -dichloropropane in ether with β -chlorovinyl-dichloroarsine; its melting point is 89–91°C. at 5 mm. (11).

Qualitative test

Nametkin and Nekrasov (20) found that when a 0.1 per cent solution of β -chlorovinyl-dichloroarsine is treated with a saturated aqueous solution of hydrogen sulfide a white amorphous precipitate of the arsine sulfide resulted, according to the reaction:



From solutions of 90 per cent alcohol the precipitate is crystalline. Using an aqueous solution of mercurous nitrate instead of the hydrogen sulfide a white precipitate was formed which turned gray in twelve hours.

Physiological properties

When β -chlorovinyl-dichloroarsine in the form of lecithin-emulsion is intravenously injected into dogs, in doses of 0.003 g. per kilogram of body weight, a violent apnea and a sudden drop in blood pressure occurs; after vagotomy, however, the compound has no effect on blood pressure or respiration (5).

β -Chlorovinylchloroarsine produces lesions on the skin similar to those caused by "mustard gas," but after a shorter time and of more serious symptoms. It is more toxic (23) and more irritating than "mustard" (24). It is a strong vesicant; its vapor is likewise vesicant and extremely irritating to the nose, throat, and bronchi, producing constitutional symptoms (17). A small quantity, even in dilute solution, applied to the skin causes painful blistering. It is also a very powerful respiratory irritant, the mucous membrane of the nose being attacked and violent sneezing induced. More prolonged exposure to the vapor leads to severe pain in the throat and chest (12).

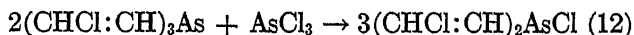
Use

Its possible use in aeroplane bombs led General Fries, former chief of Chemical Warfare Service, to apply the term "The Dew of Death" to its use in this way.

β, β' -DICHLORODIVINYLCOLOROARSINE, BIS(β -CHLOROVINYL)CHLOROARSINE,
(CHCl:CH)₂AsCl

Preparation

This compound is prepared along with the primary and tertiary arsines when acetylene is passed into arsenic trichloride containing anhydrous aluminum chloride (9, 12, 17, 18, 19, 29); by the reduction of a hot hydrochloric acid solution of β, β' -dichlorodivinyllarsinic acid with sulfur dioxide, using hydrogen iodide as a catalyst (9); by heating tris(β -chlorovinyl)-arsine and arsenic trichloride in a sealed tube at 220°C. for four hours according to the following equation:



and upon heating bis(β -chlorovinyl)dimethylarsonium iodide, (CHCl:CH)₂As(CH₃)₂I (18).

Physical properties

It is a colorless or pale yellow liquid, insoluble in water and dilute acids but soluble in all proportions in the common organic solvents. Its boiling point has been given as: 230°C. (17), 136°C. at 30 mm. (17), 130–133°C. at 26 mm. (12), 120–121°C. at 17 mm. (19), 119°C. at 15 mm. (17), 116–117°C. at 15 mm. (19), 115–116°C. at 13 mm. (9), 113°C. at 11 mm. (29), 112°C. at 10 mm. (17), 108.5–109.5°C. at 12 mm. (13), 108–109°C. at 10.5 mm. (19). Specific gravity: $d_4^{11^\circ}$, 1.7047 (13); $d_4^{20^\circ}$, 1.7020 (17); $d_4^{23.4^\circ}$, (vacuum), 1.6936 (15); $d_4^{24.1^\circ}$, (vacuum), 1.6926 (9); $d_4^{27.1^\circ}$, (vacuum), 1.6884 (9). Its index of refraction: at 11°C., $n_D = 1.6032$, $n_D = 1.6096$, $n_B =$

1.6262 (13); at 23.4°C., $n_D = 1.6014$, $n_D = 1.6080$, $n_F = 1.6250$, $n_G = 1.6401$ (15). The molecular refraction values at 11°C. for the D line of sodium and the α and β hydrogen lines are 47.47, 47.06, and 48.50, respectively (13). Vapor pressure, $\log = 9.983 - 3295.3/T$ (17).

Chemical properties

(a) *Reaction with nitric acid.* By the action of dilute nitric acid (equal volumes of concentrated acid and water) on the secondary arsine, bis(β -chlorovinyl)arsenic acid, $(\text{CHCl:CH})_2\text{AsOOH}$, is produced as colorless, needle-shaped crystals, m.p. 97°C. (12), 99°C. (19), 114–115°C. (18). It decomposes when dissolved in water (19).

(b) *Reaction with sodium hydroxide.* On treating an alcoholic solution of the secondary arsine with sodium hydroxide, bis(β -chlorovinyl)arsenious oxide, $[(\text{CHCl:CH})_2\text{As}]_2\text{O}$, is produced, m.p. 62–63°C. It is soluble in ether and hot alcohol, slightly soluble in cold alcohol, and insoluble in water (18).

(c) *Reaction with halogens.* Halogens are rapidly absorbed with the formation of additive compounds, such as $(\text{CHCl:CH})_2\text{AsClX}_2$ (12).

(d) *Reaction with potassium cyanide.* On treating an absolute alcohol solution of the secondary arsine with an aqueous solution of potassium cyanide, considerable heat is evolved and potassium chloride separates almost at once as a fine white precipitate; bis(β -chlorovinyl)arsenious cyanide, $(\text{CHCl:CH})_2\text{AsCN}$, is obtained as a colorless oil from the filtrate (18).

(e) *Reaction with hydrogen sulfide.* When hydrogen sulfide is bubbled into an absolute alcohol solution of the secondary arsine, considerable heat is evolved. The yellow-brown, viscous bis(β -chlorovinyl)arsenious sulfide, $[(\text{CHCl:CH})_2\text{As}]_2\text{S}$, separates. It is insoluble in water but soluble in alcohol. It has an extremely irritating effect on the mucous membrane. The odor is powerful, penetrating, and disagreeable (18).

(f) *Reaction with chloramine-T.* When equivalent quantities of chloramine-T and the secondary arsine are boiled together, a clear solution results from which only β, β' -dichlorodivinylarsinic acid and p-toluenesulfonamide can be isolated (19).

(g) *Reaction with methyl iodide.* When the Grignard reagent resulting from the action of methyl iodide and magnesium reacts with the secondary arsine, bis(β -chlorovinyl)methylarsine, $(\text{CHCl:CH})_2\text{AsCH}_3$, results as a thin, colorless oil, having a powerful, disagreeable odor, similar to that of the secondary arsine. It is insoluble in water, and soluble in ether and absolute alcohol. Upon heating in a sealed tube with excess of methyl iodide on a water bath, an almost solid mass of crystals is formed. At 243°C., the bis(β -chlorovinyl)dimethylarsonium iodide, $(\text{CHCl:CH})_2\text{-}$

$\text{As}(\text{CH}_3)_2\text{I}$, changed, without charring, into methyl iodide and the original arsine. The compound is soluble in water and dilute alcohol but only slightly soluble in absolute alcohol (18).

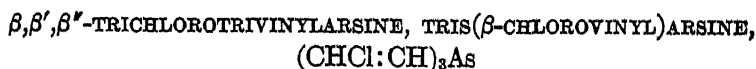
(h) *Reaction with ethyl iodide.* By the action of the Grignard reagent made from ethyl iodide and magnesium on the secondary arsine, bis(β -chlorovinyl)ethyl arsine, $(\text{CHCl:CH})_2\text{AsC}_2\text{H}_5$, a colorless oil resembling the secondary arsine in appearance and penetrating odor, is prepared. Upon heating with an excess of methyl iodide, in which it is soluble, in a sealed tube at about 90°C . for 1.5 hours, bis(β -chlorovinyl)methylethylarsonium iodide, $(\text{CHCl:CH})_2\text{As}(\text{CH}_3)\text{C}_2\text{H}_5\text{I}$, is obtained as white crystals. At 234°C . sublimation occurs with no evidence of charring or decomposition. The compound is soluble in water, alcohol, and the common organic solvents (18).

(i) *Reaction with α -bromonaphthalene.* An absolute ether solution of the secondary arsine poured into the Grignard reagent made from α -bromonaphthalene results in bis(β -chlorovinyl)- α -naphthylarsine, $(\text{CHCl:CH})_2\text{AsC}_{10}\text{H}_8$, a yellow oil, which is insoluble in water and can not be crystallized nor even fractionated at 25 mm. (18).

(j) *Reaction with benzene.* The condensation of β,β' -dichlorodivinylarsine with benzene, in the presence of anhydrous aluminum chloride, results in the formation of the hydrocarbon 9,10-dimethylantracene, m.p. $180\text{--}181^\circ\text{C}$. (8).

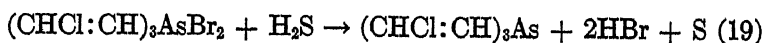
Physiological properties

Applied to the skin, the substance has vesicating properties, but is much less powerful in this respect than chlorovinyldichloroarsine. Its irritant properties on the respiratory system, on the other hand, although similar to those of chlorovinyldichloroarsine, are much more intense (12).



Preparation

This substance is prepared as the main product when acetylene is passed into arsenic trichloride containing anhydrous aluminum chloride (9, 12, 17, 18, 19, 29), but the mono- and secondary-arsines are also present. It is also made by the action of hydrogen sulfide on a chloroform solution of β,β',β'' -trichlorotrivinylarsine dibromide, in accordance with the equation:

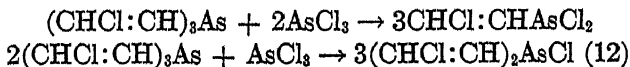


Physical properties

It is a colorless liquid, insoluble in water, dilute acids, and alcohol. In the last respect it differs from the primary and secondary chloroarsines, both of which mix in all proportions with alcohol. With the exception of alcohol, it is soluble in all the common organic solvents. Its boiling point has been given as: 260°C. (17), 162°C. at 30 mm. (17), 151–155°C. at 28 mm. (12), 145–146°C. at 18 mm. (13), 144°C. at 15 mm. (17), 144°C. at 16 mm. (19), 139–140°C. at 13 mm. (19), 138°C. at 12 mm. (29), 136.5–137.5°C. at 12 mm. (9), 136°C. at 10 mm. (17). On cooling it crystallizes in long, white needles, melting at 23°C. (19), 18°C. (9), 13°C. (29), 3–4°C. (12). Specific gravity: $d_{4,0}^{16.2^\circ}$, 1.5800 (13); $d_{4,0}^{21.5^\circ}$, 1.5727 (13); $d_{4,0}^{20^\circ}$, 1.5720 (17); $d_{4,0}^{22^\circ}$ (vacuum), 1.5685 (9); $d_{4,0}^{23.7^\circ}$ (vacuum), 1.5664 (15); $d_{4,0}^{26.3^\circ}$ (vacuum), 1.5631 (9). Index of refraction: $n_\alpha = 1.5925$ (16.2°C.), $n_D = 1.5985$ (16.2°C.), $n_D = 1.5942$ (21.5°C.), $n_\beta = 1.6140$ (16.2°C.) (13); at 23.7°C., $n_C = 1.5939$; $n_D = 1.6005$; $n_F = 1.6158$ (15). The molecular refraction: $MR_\alpha = 55.62$ (16.2°C.), $MR_D = 56.07$ (16.2°C.), $MR_D = 56.01$ (21.5°C.), $MR_\beta = 57.24$ (16.2°C.) (13). Vapor pressure, $\log = 9.159 - 3312.43/T$ (17).

Chemical properties

(a) *Reaction with arsenic trichloride.* When it is heated with arsenic trichloride at 200–220°C. and the product is fractionated, a mixture of both chlorovinylchloroarsine and dichlorodivinylchloroarsine is obtained, the amount depending upon the proportions of trichlorotrivinylarsine and arsenic trichloride used; when the ratio of arsenic trichloride and trichlorotrivinylarsine is 45.3:54.7, the proportion of chlorovinylchloroarsine and dichlorodivinylchloroarsine is 33.55 per cent and 41.34 per cent respectively (25.11 per cent being arsenic trichloride remaining unattacked); when the ratio of arsenic trichloride and the tertiary arsine is 58.24:41.76, the proportion of the primary and secondary arsines is 48.16 per cent and 16.25 per cent respectively (35.59 per cent being unattacked arsenic trichloride) (12). The reactions may be expressed as follows:



(b) *Reaction with nitric acid.* On heating the tertiary arsine with concentrated nitric acid, β,β',β'' -trichlorotrivinylhydroxyarsonium nitrate, $(\text{CHCl:CH})_3\text{As}(\text{OH})\text{NO}_3$, forms as an oily layer that separates on the bottom of the vessel but which crystallizes quickly when a little water is added. The white crystals are soluble in cold absolute alcohol and hot water. They melt at 103°C. (16, 17). When an aqueous solution of the nitrate is treated with an equivalent quantity of sodium hydroxide, the

solution extracted with chloroform, and the chloroform solution evaporated, a crystalline residue of β,β',β'' -trichlorotrivinylarsenic oxide, $(\text{CHCl:CH})_3\text{AsO}$, is formed. It separates on crystallization from benzene containing a little carbon tetrachloride, in long colorless needles or in small plates which melt with decomposition at 154°C . (19).

(c) *Reaction with bromine.* When a ligroin solution of the tertiary arsine in a freezing mixture is cautiously treated with a ligroin solution of bromine, β,β',β'' -trichlorotrivinylarsine dibromide, $(\text{CHCl:CH})_3\text{AsBr}_2$, separates in colorless needles which melt at 107°C . (19).

(d) *Reaction with methyl iodide.* On heating trichlorotrivinylarsine with an equimolecular proportion of methyl iodide in a sealed tube on a water bath at 80°C . for twenty-two hours and then at 100°C . for two hours (16) or at 100°C . for twenty-seven hours (17) β,β',β'' -trichlorotrivinyl-methylarsonium iodide, $(\text{CHCl:CH})_3\text{AsCH}_3\text{I}$, is formed. The contents of the tube become almost solid with a mass of needle-shaped crystals which are very slightly soluble in absolute alcohol, either hot or cold, but dissolve readily in 95 per cent alcohol and in water; the melting point has been given as 202°C . (18) and 209°C . (19).

(1) *Double salt formed with mercuric iodide.* Molecular proportions of the two iodides are dissolved separately in alcohol and then mixed and warmed for a short time. As the solution cools a heavy, granular, light yellow precipitate is formed, $(\text{CHCl:CH})_3\text{AsCH}_3\text{I} \cdot \text{HgI}_2$, which, when recrystallized from alcohol, melts between 150°C . and 156°C . It is soluble in hot absolute alcohol, somewhat soluble in hot 95 per cent alcohol, and insoluble in cold absolute alcohol and in hot and cold water (18).

(2) *Double salt formed with phenylmagnesium iodide.* Molecular proportions of the two iodides, the arsonium iodide dissolved in absolute alcohol, are heated in a sealed tube for twelve hours at 90°C . Long, thick, needle-like, yellow crystals of $(\text{CHCl:CH})_3\text{AsCH}_3\text{I} \cdot \text{C}_6\text{H}_5\text{HgI}$ form when the contents of the tube are allowed to cool. It is soluble in warm, absolute alcohol and insoluble in water; its melting point is not sharp but is near 147 – 148°C . (18).

(e) *Reaction with benzene.* The condensation of the tertiary arsine with benzene in the presence of anhydrous aluminum chloride results in the formation of the hydrocarbon, 9,10-dimethylantracene, m.p. 180 – 181°C . (8).

(f) *Reaction with chloramine-T.* When an acetone solution of the tertiary arsine is boiled with chloramine-T for twenty minutes, filtered, and the filtrate evaporated to dryness, colorless plates of β,β',β'' -trichlorotrivinylarsine-*p*-toluenesulfonylimine, $(\text{CHCl:CH})_3\text{As:NSO}_2\text{C}_6\text{H}_4(\text{CH}_3) \cdot \text{H}_2\text{O}$, result, m.p. 124°C . (19).

(g) *Reaction with metallic compounds.* (1) *With silver nitrate.* The

double salts of trichlorotrivinylarsine and silver nitrate, $(\text{CHCl:CH})_3\text{-As}\cdot\text{AgNO}_3$ and $[(\text{CHCl:CH})_3\text{As}]_2\cdot\text{AgNO}_3$, are prepared by dissolving separately the tertiary arsine and silver nitrate in absolute alcohol and adding an excess of the latter to the former. Long, fine, silky needles form at once in such quantity that the solution becomes thick and semi-solid; the crystals melt at 144°C . In hot water the crystals melt and form an oil which, on cooling, quickly crystallizes again, but in the form of short, thick, needle-like crystals. The compounds are stable toward light when pure and dry (18).

(2) *With potassium aurichloride.* On adding an alcoholic solution of potassium aurichloride to a cooled alcoholic solution of the tertiary arsine, the mixture rapidly becomes colorless and then slowly deposits small, heavy, white crystals of β,β',β'' -trichlorotrivinylarsine aurichloride, $(\text{CHCl:CH})_3\text{As}\cdot\text{AuCl}$, which melt at 123°C . with decomposition. When the colorless crystals are exposed to light for several days, they gradually acquire a purplish-gray color (19).

(3) *With palladous chloride.* When an alcoholic solution of palladous chloride is added to a cooled alcoholic solution of the tertiary arsine, long, yellowish-brown needles of bis(β,β',β'' -trichlorotrivinylarsine) palladichloride, $[(\text{CHCl:CH})_3\text{As}]_2\text{PdCl}_2$, begin to form within a few seconds; these are soluble in ether and acetone, and melt at 196°C . with decomposition. The formation of this characteristic compound furnishes a ready means for detecting the presence of the tertiary arsine (19).

(4) *With chloroplatinic acid.* When a dilute alcoholic solution of chloroplatinic acid is added to an alcoholic solution of the tertiary arsine, long, very pale yellow needles of platinum bis(β -chlorovinyl)-bis(β,β',β'' -trichlorotrivinyl)arsine, $[(\text{CHCl:CH})_3\text{As}]_2\text{Pt}(\text{CHCl:CH})_2$, separate, followed later by short, lemon-yellow prisms; on recrystallizing from alcohol, very pale yellow, almost white, needles separate, m.p. 198°C . (19).

Physiological properties

Trichlorotrivinylarsine is neither a strong vesicating agent nor a powerful respiratory irritant. At the same time its odor is pungent and most unpleasant, and induces violent sneezing (12).

REFERENCES

- (1) ANONYMOUS: Gasschutz u. Luftschutz, 2, 264 (1932).
- (2) BAUD: Compt. rend. 130, 1319-22 (1900).
- (3) BURTON AND GIBSON: J. Chem. Soc. 1926, 464-70.
- (4) DAFERT: Monatsh. 40, 313-23 (1919).
- (5) FEGLER: Compt. rend. soc. biol. 100, 218-21 (1929).
- (6) FISCHER: Ann. 403, 106-17 (1914).
- (7) GANGLOFF AND HENDERSON: J. Am. Chem. Soc. 39, 1420-7 (1917).

- (8) GIBSON AND JOHNSON: J. Chem. Soc. **1930**, 2785-6.
- (9) GIBSON AND JOHNSON: J. Chem. Soc. **1931**, 753-6.
- (10) GIBSON AND POPE: J. Chem. Soc. **117**, 271-8 (1920).
- (11) GORSKIĬ, SHPANSKIĬ, AND MULYAR: Ber. **67**, 730-5 (1934).
- (12) GREEN AND PRICE: J. Chem. Soc. **119**, 448-53 (1921).
- (13) GRYSZKIEWICZ-TROCHIMOWSKI AND SIKORSKI: Bull. soc. chim. **41**, 1750-85 (1927).
- (14) HERBST: Kolloidchem. Beihefte **23**, 313-44 (1926).
- (15) JOHNSON: Ber. **65**, 294-302 (1932).
- (16) KRETOV AND BERLIN: J. Gen. Chem. U.S.S.R. **1**, 411-8 (1931).
- (17) LEWIS AND PERKINS: Ind. Eng. Chem. **15**, 290-5 (1923).
- (18) LEWIS AND STIEGLER: J. Am. Chem. Soc. **47**, 2546-56 (1925).
- (19) MANN AND POPE: J. Chem. Soc. **121**, 1754-9 (1922).
- (20) NAMETKIN AND NEKRASOV: Z. anal. Chem. **77**, 285-9 (1929).
- (21) NEKRASOV AND NEKRASOV: Ber. **61**, 1816-21 (1928).
- (22) ROVIDA: Sperimentale **80**, 5-24 (1926).
- (23) ROVIDA: Sperimentale **83**, 101-13 (1929).
- (24) ROVIDA: Sperimentale **83**, 114-20 (1929).
- (25) SCHERLIN AND EPSTEIN: Ber. **61**, 1821-5 (1928).
- (26) SHIVER: J. Chem. Education **7**, 95-108 (1930).
- (27) STOLTZENBERG: Was Jeder vom Gaskampf und den chemischen Kampfstoffen wissen sollte. Hamburg (1930).
- (28) VEDDER: The Medical Aspects of Chemical Warfare. The Williams & Wilkins Co., Baltimore (1925).
- (29) WIELAND: Ann. **431**, 30-40 (1923).

